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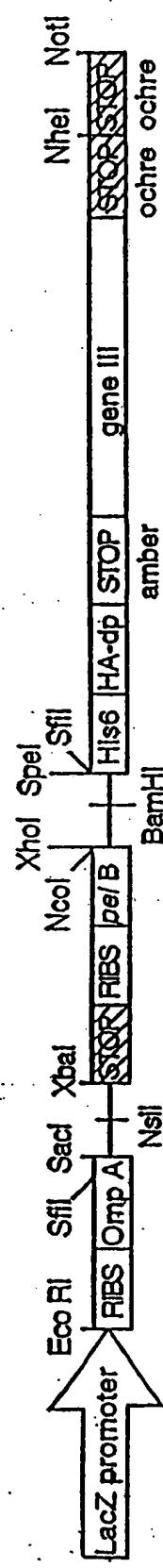


Fig. 1

Human Antibody sequence (TT sequence) (SEQ ID NO: 54)

Heavy Chain: cloning sites *Xho* I and *Spe* I are underlined

1 11
gag gtg cag ctg CTC GAG CAG TCT GGG GCT GAG GTG AAG AAG CCT GGG TCC TCG GTG AAG
glu val gln leu leu glu gln ser gly ala glu val lys lys pro gly ser ser val lys
21 31
GTC TCC TGC ACG GCT TCT GGA GGC ACC TTC AAC AAC TAT TAT GCC ATC AGC TGG GTG CGA CAG
val ser cys arg ala ser gly gly thr phe asn asn tyr ala ile ser trp val arg gln
41 51
GCC CCT GGA CAA CGG CTT GAG TGG ATG GGA GGG ATC TTC CCT TTC CGT AAT ACA GCA AAG
ala pro gly gln gly leu glu trp met gly gly ile phe pro phe arg asn thr ala lys
61 71
TAC GCA CAA CAC TTC CAG GGC AGA GTC ACC ATT ACC GCG GAC GAA TCC ACG GGC ACA GGC
tyr ala gln his phe gln gly arg val thr ile thr ala asp glu ser thr gly thr ala
81 91
TAC ATG GAG CTG ACG AGC CTG AGA TCT GAG GAC ACG GCC ATA TAT TAT TGT GCG AGA GCG
tyr met glu leu ser ser leu arg ser glu asp thr ala ile tyr tyr cys ala arg gly
101 111
GAT ACG ATT TTT GCA GTC ACC ATG GGA TAC TAC GCT ATG GAC GTC TGG GGC CAA GGG ACC
asp thr ile phe gly val thr met gly tyr tyr ala met asp val trp gly gln gly thr
121 131
ACG GTC ACC GTC TCC GCA GCC TCC ACC AAG GGC CCA TCG GTC TTC CCC CTG GCA CCC TCC
thr val thr val ser ala ala ser thr lys gly pro ser val phe pro leu ala pro ser
141 151
TCC AAG AGC ACC TCT GGG GGC ACA GCG GGC CTG GGC TGC CTG GTC AAG GAC TAC TTC CCC
ser lys ser thr ser gly gly thr ala ala leu gly cys leu val lys asp tyr phe pro
161 171
GAA CGG GTG ACG GTG TCG TGG AAC TCA GGC GCC CTG ACC AGC GGC GTG CAC ACC TTC CGG
glu pro val thr val ser trp asn ser gly ala leu thr ser gly val his thr phe pro
181 191
GCT GTC CTA CAG TCC TCA GGA CTC TAC TCC CTC AGC AGC GTG GTG ACC ACC CCC TCC AGC
ala val leu gln ser ser gly leu tyr ser leu ser ser val val thr val pro ser ser
201 211
AGC TTG GGC ACC CAG ACC TAC ATC TGC AAC GTG AAT CAC AAG CCC AGC AAC ACC AAG GTG
ser leu gly thr gln thr tyr ile cys asn val asn his lys pro ser asn thr lys val
221 231
GAC AAG AAA GTT GAG CCC AAA TCT TGT GAC AAA act act
asp lys lys val glu pro lys ser cys asp lys thr ser

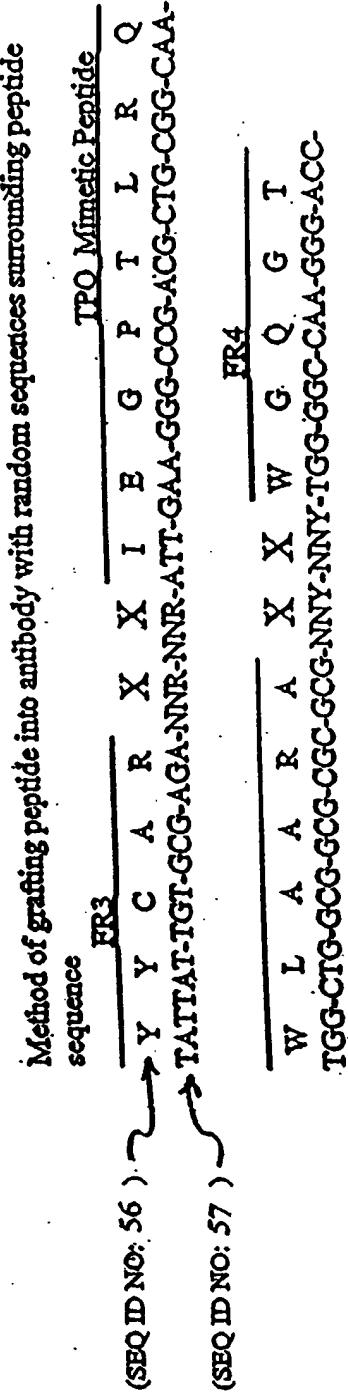
Fig. 2A

Human Antibody Sequence (TT sequence) (SEQ ID NO: 55)

Light Chain: cloning sites *Sac I* and *Xba I* are underlined

1 gaa ctc acg cag tct cca ggc acc ctg tct ttg tct cca ggg gaa aga gcc acc ctc tcc
glu leu thr gln ser pro gly thr leu ser leu ser pro gly glu arg ala thr leu ser
21 11
tgc agg gcc agt cac agt gtt agc agg gcc tac tta gcc tgg tac cag cag aaa cct ggc.
cys arg ala ser his ser val ser arg ala tyr leu ala trp tyr gln gln lys pro gly
41 31
cag gct ccc agg ctc ctc atc tat ggt aca tcc agc agg gcc act ggc atc cca gac agg
gln ala pro arg leu leu ile tyr gly thr ser ser arg ala thr gly ile pro asp arg
61 51
ttc agt ggc agt ggg tct ggg aca gac ttc act ctc acc atc agc aga ctg gag cct gaa
phe ser gly ser gly ser gly thr asp phe thr leu thr ile ser arg leu glu pro glu
81 71
gat ttt gca gtg tac tac tgt cag cag tat ggt ggc tca ccg tgg ttc ggc caa ggg acc
asp phe ala val tyr tyr cys gln gln tyr gly ser pro trp phe gly gln gly thr
101 111
AAG GTG GAA CTC AAA CGA ACT GTG GCT GCA CCA TCT GTC TTC ATC TTC CCG CCA TCT GAT
lys val glu leu lys arg thr val ala ala pro ser val phe ile phe pro pro ser asp
121
GAG CAG TTG AAA TCT GGA ACT GCC TCT GTT GTG TGC CTG CTG AAT AAC TTC TAT CCC AGA
glu gln leu lys ser gly thr ala ser val val cys leu leu asn asn phe tyr pro arg
141 131
GAG GCC AAA GTA CAG TGG AAG GTG GAT AAC GCC CTC CAA TCG GGT AAC TCC CAG GAG AGT
glu ala lys val gln trp lys val asp asn ala leu gln ser gly asn ser gln glu ser
161 151
GTC ACA GAG CAG GAC AGC AAG GAC AGC ACC TAC AGC CTC AGC AGC ACC CTG ACG CTG AGC
val thr glu gln asp ser lys asp ser thr tyr ser leu ser ser thr leu thr leu ser
181 171
AAA GCA GAC TAC GAG AAA CAC AAA GTC TAC GCC TGC GAA GTC ACC CAT CAG GGC CTG AGC
lys ala asp tyr glu lys his lys val tyr ala cys glu val thr his gln gly leu ser
201 191
TTG CCC GTC ACA AAG AGC TTC AAC AGG GGA GAG TGT TAG Ttc tag a
leu pro val thr lys ser phe asn arg gly glu cys AMB 211

Fig. 2B



The TPO mimetic peptide was grafted into the heavy chain CDR3 region of the tetanus toxoid antibody. The peptide was flanked on either side by two random amino acids, shown as "X" in the figure.

Fig. 3

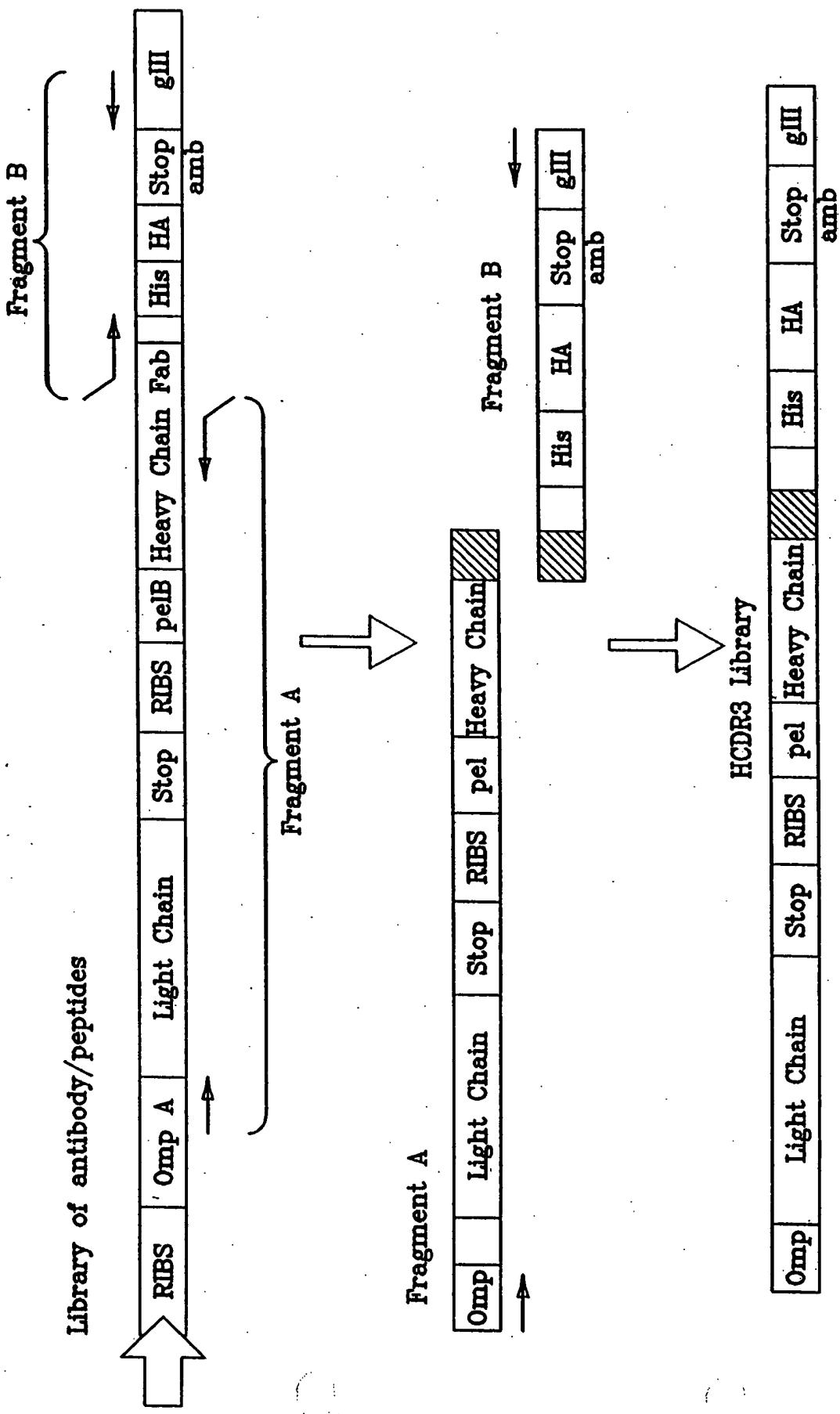


FIG. 4

AMINO ACID SEQUENCE

SEQ ID NO.

<u>CLONE</u>	<u>SEQ ID NO.</u>
X1a	Pro-Pro-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Gly-Gly- CCG-CCC-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GCG-GGA-GGC 25 26
X1a-11	Gly-Gly-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Gly-Gly- GGG-GGT-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GGC-GGA 27 28
X1a-13	Gly-Gly-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Gly-Gly- GGC-GGT-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GGA-GGC 29 30
X1c	Trp-Leu-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Pro-Val TGG-CTG-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GCG-GCT-GTC 31 32
X2a	Met-Ile-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Val-Gly- ATG-ATA-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GCG-GTT-GGC 33 34
X3a	Val-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Pro-Val TGG-GTA-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GCG-CCT-GTT 35 36
X3b	Gly-Pro-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Pro-Asp GGG-CCG-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GCG-CCC-GAT 37 38
X4b	Leu-Pro-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Pro-Val TTG-CCA-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GCG-CCT-GTT 39 40
X4c	Ser-Leu-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Pro-Val TCA-CTG-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GCG-CCC-ATC 41 42
X5a	Thr-Met-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Pro-Val ACA-ATG-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GCG-CCC-GTT 43 44
X5c	Thr-Thr-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Pro-Val ACG-ACA-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GCG-CCT-GTC 45 46
X7a	Thr-Ala-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Cys-Ser ACA-CCG-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GCG-TGC-AGC 47 48
X7b	no peptide deletion mutant
X7c	Gln-Thr-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Pro-Asp CAG-ACA-ATT-GAA-GGG-CCG-ACG-CTG-CGG-CAA-TGG-CTG-GCG-GCG-GCG-CCT-GAC 49 50

Fig. 5

pRL8

(SEQ ID NO: 60)

→ GGGAAATTGTAAGCGTTAATTTTGTAAAATTGCGTTAAATTGGTTAA.
ATCAGCTCATTTTAACCAATAGGCCGAAATCGCAAAATCCCTTATAAAATC
AAAAGAATAGACCGAGATAGGGTTGAGTGTGTTCCAGTTGGAACAAGAGT
CCACTATTAAAGAACCGTGGACTCCAACGTCAAAGGGCGAAAACCCTCTATC
AGGGCGATGGCCCACATACGTGAACCATCACCTAATCAAGTTTTGGGTGTC
GAGGTGCGTAAAGCACTAAATCGGAAACCTAAAGGGAGCCCCCGATTTAGA
GCTTGACGGGAAAGCCGGCGAACGTGGAGAAAAGGAAGGGAAAGAAAGC
GAAAGGAGCGGGCGTAGGGCGCTGGCAAGTGTAGCGGTACGCTGCGCGT
AACCAACACACCGCCGCGCTTAATGCGCCGCTACAGGGCGCGTCAGGTGGC
ACTTTTGGGAAATGTGCGCGAACCCCTATTGTTTATTTCTAAATA
TTCAAATATGTATCCGCTCATGAGACAATAACCCGATAAATGCTTCAATAAT
ATTGAAAAGGAAGAGTATGAGTATTCAACATTCCGTGCGCCCTTATTCC
TTTTTGGGCATTGGCTTCCGTGTTTGTCAACCCAGAAAACGCTGGTGA
GTAAAAGATGCTGAAGATCAGTTGGGTGACGAGTGGGTTACATCGAACTGG
ATCTCAACAGCGGTAAAGATCCTGAGAGTTTCCGCCCCGAAAGAACGTTTCCA
ATGATGAGCACTTTAAAGTTCTGCTATGTGGCGCGTATTATCCCGTATTGA
CGCCGGCAAGAGCACTCGTCGCCGATACACTATTCTCAGAAATGACTTG
GTTGAGTACTCACCAGTCACAGAAAAGCATCTACGGATGGCATACAGTAA
GAGAATTATGCACTGCTGCCATAACCATGAGTGATAACACTGCGGCCACTT
ACTTCTGACAACGATCGGAGGACCGAAGGAGCTAACCGCTTTTGACAAAC
ATGGGGGATCATGTAACCTGCCCTGATGTTGGGAAACCGGAAGCTGAATGAAG
CCATACCAAACGACGAGCTGTACACCACGATGCTGTAGCAATGGCAACAAC
GTTGCGCAAACATATTAACTGGCGAACTACTTACTCTAGCTTCCCGGCAACAAAT
TAATAGACTGGATGGAGGCGGATAAAGTTGCAAGGACCACTCTGCGCTCGGC
CCTTCCGGCTGGCTGGTTATTGCTGATAAAATCTGGAGCCGGTGAGCGTGGGT
CTCGCGGTATCATTGCACTGGGCCAGATGTTAAGCCCTCCCGTATCGT
AGTTACTACACGACGGGGAGTCAGGCAACTATGGATGAACGAAATAGACA
GATCGCTGAGATAGGTGCTCACTGATTAAGCATGGTAACTGTCAGACCAA
GTTTACTCATATATACTTTAGATTGATTAAAACCTCATTTTAATTAAAAGG
ATCTAGGTGAAGATCTTCTTGTATAATCTCATGACCAAAATCCCTAACGTGA
GTTTCTGTTCCACTGAGCGTCAGACCCCGTAGAAAAGATCAAAGGATCTCTT
GAGATCCTTTCTGCGCGTAATCTGCTGTTGCAAACAAAAACCGACCG
CTACCAAGCGGTGGTTGTTGCCGATCAAGAGCTACCAACTCTTCCGAA
GGTAACTGGCTTCAGCAGAGCGCAGATACCAAAACTGTCTTCTAGTGTAG
CCGTAGTTAGGCCACCACTCAAGAACTCTGTAACGCCACCGCTACATACCTCGC
TCTGCTAATCCTGTTACCAAGTGGCTGCTGCCAGTGGCGATAAGTCGTGCTTA
CCGGGTGGACTCAAGACGATAGTTACCGATAAGGCCAGCGGGTGGCTG
AACGGGGGGTTGCGACACAGCCAGCTGGAGCGAACGACCTACACCGA

Fig. 6A

ACTGAGATACCTACAGCGTGAGCTATGAGAAAGCGCCACGCTTCCGAAGGG
AGAAAGGCGGACAGGTATCCGTAAGCGGCAOGGTGCGAACAGGAGAGCGC
ACGAGGGAGCTCCAGGGGAAACGCCTGGTATCTTATAGTCTGTGCGGT
TTCGCCACCTCTGACTTGAGCGTCGATTTGATGCTCGTCAGGGGGCGG
AGCCTATGGAAAAACGCCAGCAACGCCCTTTACGGTCTGGCCTTTG
CTGGCTTTGCTCACATGTTCTTCCTGCGTATCCCCTGATTCTGTGGATAA
CCGTATTACGCCCTTGAGTGAGCTGATACCGCTGCCAGCCGAACGACC
GAGCGCAGCAGTCAGTGAGCGAGGAAGCGGAAGAGCGCCAAATACGCAA
CCGCCCTCTCCCCGCGCGTGGCGATTCAATTATGCACTGGCACAGAGTT
TCCCGACTGGAAAGCGGGCAGTGAGCGAACCGCAATTAAATGTGAGTTAGTC
ACTCATTAGGCACCCAGGCTTACACTTATGCTCTGGCTCGTATGTTGTG
TGGAATTGTGAGCGGATAACAATTGAATTCAAGGAGGAATTAAAATGAAAAA
GACAGCTATCGCGATTGCACTGGCACTGGCTGGCTACCGTGGCCAG
GCCGCCGAGCTCGGCCATGGCTGGTGGCGAGCAGTAATAACAATCCAGCG
GCTGCCGTAGGCAATAGGTATTCATTATGACTGTCCTGGCACTAGCTA
GTTAGAATTGTAATCATGGCATAGCTGTTCTGTGTGAAATTGTTATOC
GCTCACAAATTCCACACAACATACGAGCCGGAAGCATAAAAGTGTAAAGCCTGG
GGTGCCTAATGAGTGAGCTAACACATTAATGCGTTCGCTCACTGCCGC
TTTCCAGTCGGAAACCTGTCGTGTTACTAATGATGGTGTGGTAGGGCTAG
TTTGTCAACAAGATTGGCTCAACTTCTGTCACCTTGGTGTGGCTGGCT
TGTGATTACGTTGCAGATGTAGGTCTGGTGGCCAAAGCTGCTGGAGGGCAC
GGTCACCACGCTGCTGAgGGAGTAGAGTCCTGAGGACTGTAGGACAGCCGGG
AAGGTGTGCA CGCCGCTGGTCAgGGCCCTGAgTTCCACGACACGTCGCCGG
TTCgGGGAAGTAGTCCTGACCAAGGCAAGCCCAGGGCCGTGCCCCCAGAG
GTGCTCTGGAGGAGGGTGCAGGGGAAGACCGATGGCCCTGGTGGAG
GCTGCCGAGACGGTACCGTGCTTACAGCAGAAACCTGGCCAGGCTCCAG
GCTCCTCATCTATGGTACATCCAGCAGGCCACTGGCATCCCAGACAGGTTC
AGTGGCAGTGGCTGGACAGACTTCACTCTCACCATCAGCAGACTGGAGC
CTGAAGATTGCACTGACTACTGTCAGCAGTATGGTGGCTACCGTGGTTC
GGCCAAGGGACCAAGGTGGAACCTAAACGAACGTGGCTGCACCATCTGCT
TCATCTCCGCCATCTGATGAGCAGTGAATCTGAAACTGCCCTGTGTTG
TGCCTGCTGAATAACTCTATCCCAGAGAGGGCAAAAGTACAGTGGAAAGGTGG
ATAACGCCCTCCAATGGGTAACTCCAGGAGAGTGTACAGAGCAGGACAG
CAAGGACAGCACCTACAGCCTCAGCAGCACCTGACGCTGAGCAAAGCAGA
CTACGAGAAACACAAAGTCTACGCCCTGCGAAGTCaccatcaggcgttagtgcggcgtcac
aaagagcgtcaacggaggaggttaatTCTAGATAATTAGGAGGAATTAAAATGAA
ATACCTATTGCTACGGCAGCCGCTGGATTGTTATTACTGCTGCCAACAG
CCATGGCCGAGGTGCAGCTGCTGAGATGAGCGATAAAATTATTCACCTGAC
TGACGACAGTTTGACACGGATGTACTCAAAGCGGACGGGGCGATCTCGTC
GATTCTGGCAGAGTGGTGGTCCGTGCAAAATGATGCCCGATTCTGG
ATGAAATCGCTGACGAATATCAGGGAAACTGACCGTGTGCAAAACTGAACAT
CGATCAAAACCCCTGGCACTGCGCCGAAATATGGCATCCGTGGTATCCCGACT
CTGCTGCTGTTCAAAAACGGTGAAGTGGCGGCAACCAAAGTGGGTGCACTTG
TCTAAAGGTCA GTGAAAGAGTTCCTCGACGCTAACCTGGCGTACCCGTACG
ACGTTCCGGACTACGGTCTACTAGTccgaaaccgtcacccacgggcttccigcggtggccgc
atcgcccgltcggaggaaaaaglgaaaaacccgtgaaagctcagaactccgagctggcgtccacigccaaatgcigcgcaac

Fig. 6B

aggtggcacagctgaaacagaaaatgtaccatggcggtgtgctagt GGCCAGGCCGCCACCCACAT
CACCATCACCATGGCGCATACCGTACGACGTTCCGGA
CTACCGCTCTGAGGGAGG
AGGGTGGTGGCTCTGAGGGTGGCGGTCTGAGGGTGGCGGCTCTGAGGGAGG
CGGTTCCGGTGGCTCTGGTTCCGGTGATTTGATTATGAAAAGATGGCAA
ACGCTAATAAGGGGCTATGACCGAAAATGCCGATGAAAACGCGCTACAGTC
TGACGCTAAAGGCAAACCTGATTCTGCGCTACTGATTACGGTGTGCTATCG
ATGGTTTCATTGGTGACGTTCCGGCTTGCTAATGGTAATGGTGCTACTGGT
GATTTGCTGGCTCTAATTCCCAAATGGCTCAAGTCGGTGACGGTGATAATTG
ACCTTTAATGAATAATTCCGTCAATATTACCTTCCCTCCCTCAATCGGTTGA
ATGTCGCCCTTTGCTTTAGCGCTGGTAAACCATATGAATTCTATTGATTG
TGACAAAATAAACTTATTCCGTGGTGTCTTGCGTTCTTTATATGTTGCCAC
CTTATGTATGTATTCTACGTTGCTAACATACTGCGTAATAAGGAGTCTA
AGCTAGCTAATTAAATTAAAGCGGCCGAGATCT

Fig. 6C

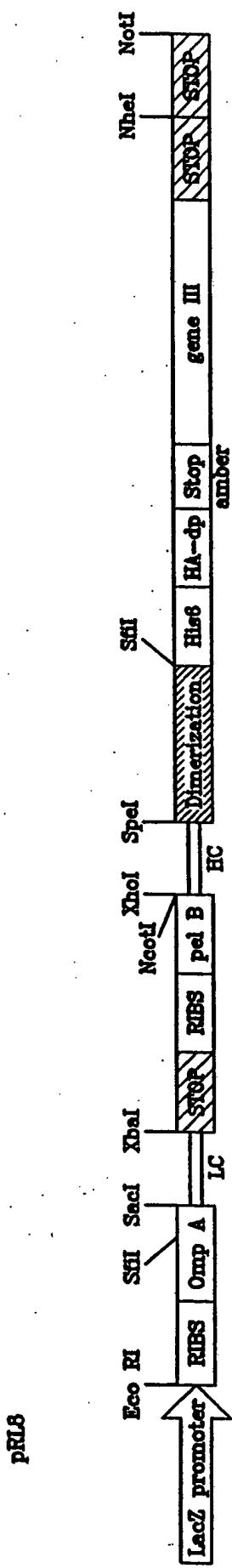


FIG. 7

(SEQ ID NO: 52.) ^{SpeI} → ACTACTCCGAAACCGTCTACCCACGGGCTCTCTCCGGCATGCCGTGGCTCTGAGGAAAAGTCAAACCTGAGACTCAGAACTCCGAGCTGGGTCCACTGCCA 115

(SEQ ID NO: 53.) → P K P S T P P G S S S C G G R I A R L E E K V K. T. L K A O N S E L A S T A _{Jun dimerization domain}

(SEQ ID NO: 54.) → P K P S T P P G S S S C G G R I A R L E E K V K. T. L K A O N S E L A S T A _{Jun dimerization domain}

StI I

ACATGCTGCCGAAACGGTCAAGCTGAAACAGAAAAGTTATGAAACATGGGGTGTGCTAGTGGCAAGGACATACCCATACCCATGCCGCAATACCCGTACCA 230

N H L R E Q V A O L K Q K V H N H G G C A S G O A G O H H H H H G A Y P Y D _{His6 Tag}

CGTTCCGGACTACGGCTCTTAGGAGGTGGCTCTGAG 270

V P D Y A S . . . _{—HA tag and Amber stop —}

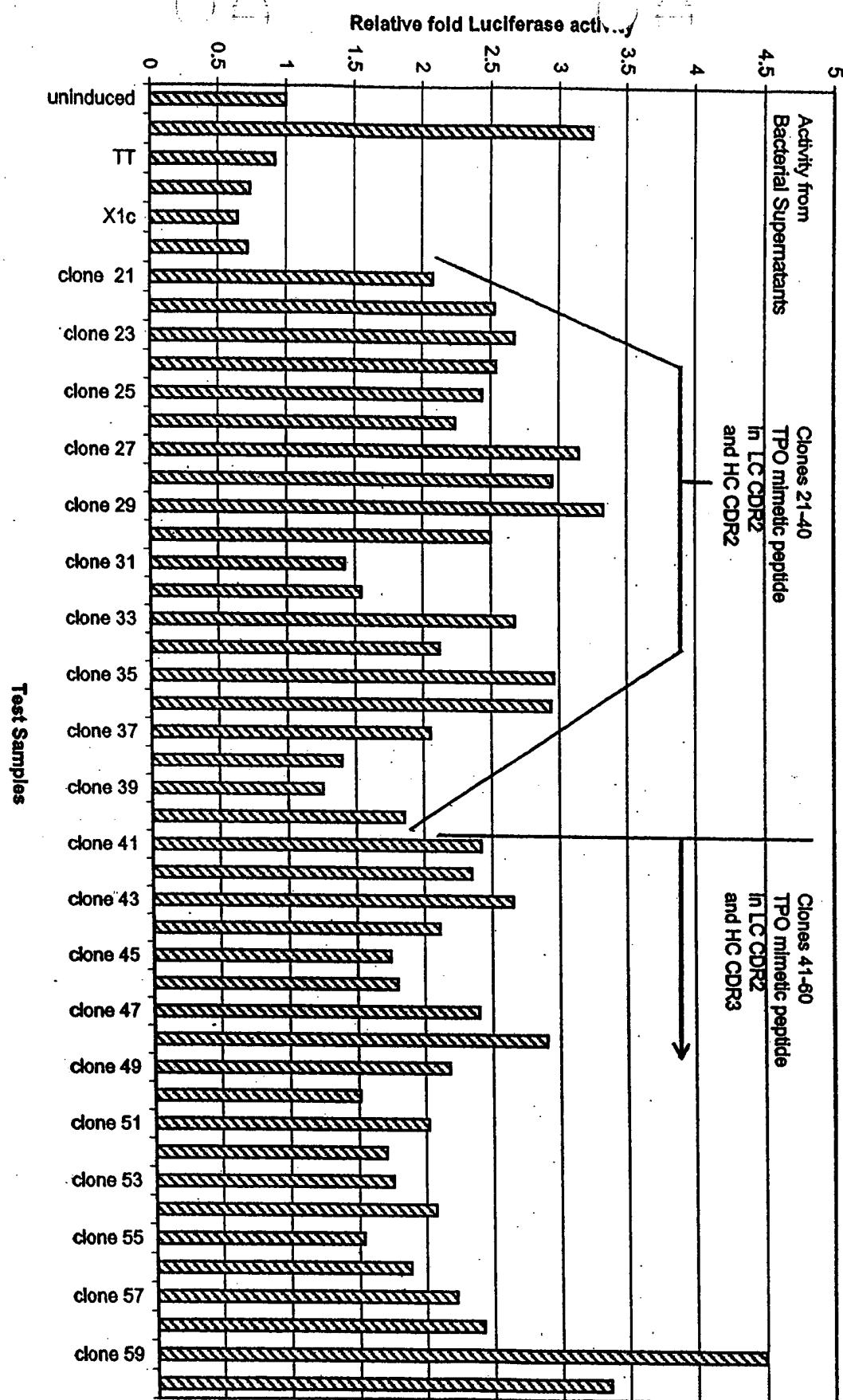
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TPO Positive Clones nnk nnk nnk nnk
 1 2 IEGPTLROWLAARA 3 4

	Sample	nnk nnk		nnk nnk		Amino Acids		Amino Acids	
		1	2	3	4	1	2	3	4
HC CDR3	X1c	tgg	ctg	cct	gtc	Trp	Leu	Pro	Val
	X3a	gtg	gta	cct	gtt	Val	Val	Pro	Val
	X3b	ggg	ccg	ccc	gat	Gly	Pro	Pro	Asp
	X4b	ttg	cca	cct	gtt	Leu	Pro	Pro	Val
	X4c	tca	ctg	ccc	atc	Ser	Leu	Pro	Ile
	X5a	aca	atg	ccc	gtt	Thr	Met	Pro	Val
	X5c	acg	aca	cct	gtc	Trp	Leu	Pro	Val
	X7c	cag	aca	cct	eac	Gln	Thr	Pro	Asp
HC CDR2	24	ctt	tat	tct	aat	Leu	Tyr	Ser	Asn
	39	act	tac	ttt	cat	Thr	Tyr	Leu	His
	3	agg	atg	ctt	gag	Arg	Met	Leu	Glu
	7	aag	gaa	tct	aag	Lys	Glu	Ser	Lys
	8	gcg	cat	gtg	cag	Ala	His	Val	Gln
	10	cag	gag	att	agt	Gln	Glu	Ile	Ser
	11	cgg	aat	aat	ccg	Arg	Asn	Asn	Pro
	19	cag	cta	aat	tct	Gln	Leu	Asn	Ser
	25	agt	att	ttt	gtc	Ser	Ile	Phe	Val
	28	ggg	ccc	act	agt	Gly	Pro	Thr	Ser
LC CDR1	10	aag	ggt	gtt	agt	Lys	Gly	Val	Ser
	11	cat	ggg	gtg	gct	His	Gly	Val	Ala
	12a	cgt	acg	atg	gct	Arg	Thr	Met	Ala
	12b	cgt	ggt	gtt	aat	Arg	Gly	Val	Asn
	14	cgt	tcg	ctt	gcg	Arg	Ser	Leu	Ala
	16	cgg	ggt	gtt	gcg	Arg	Gly	Val	Ala
	18	agg	acg	gtg	tct	Arg	Thr	Val	Ser
	47	aag	ggg	gtg	gcg	Lys	Gly	Val	Ala
LC CDR2	1	aat	ccg	agg	ggt	Asn	Pro	Arg	Gly
	2	tcg	cct	ccg	agt	Ser	Pro	Arg	Ser
	3	tcg	cct	cgt	acg	Ser	Pro	Arg	Thr
	4	tcg	cct	tgg	cgt	Ser	Pro	Trp	Arg
	5	act	ccg	aat	tgg	Thr	Pro	Asn	Trp
	6	aat	cct	gcg	agg	Asn	Pro	Ala	Arg
	7	aat	ccg	tcg	ggg	Asn	Pro	Ser	Gly
	9	aat	cct	tat	tag	Asn	Pro	Tyr	Stop
	10	aat	ccg	ccg	tct	Asn	Pro	Arg	Ser
	11	aat	ccg	gat	gtg	Asn	Pro	Asp	Val
	12	tcg	ccg	tcg	ccg	Ser	Pro	Ser	Arg
	13	aat	cct	ctg	ttt	Asn	Pro	Leu	Phe
	14	aat	ctt	ggg	tat	Asn	Pro	Gly	Tyr
	15	aat	cct	att	agt	Asn	Pro	Ile	Ser
	16	aat	cct	cag	cgg	Asn	Pro	Gln	Arg
	18	aat	ccg	ccg	acg	Asn	Pro	Arg	Thr
	19	aat	ccg	cgt	ggg	Asn	Pro	Arg	Gly
	20	cat	ttg	aga	ctg	His	Leu	Arg	Leu
	21	aag	tag	att	tat	Lys	Stop	Ile	Tyr
	23	aat	cct	ggt	aag	Asn	Pro	Gly	Lys
	24	aat	cct	cgt	ggg	Asn	Pro	Arg	Gly
	26	aat	cct	aat	gtg	Asn	Pro	Asn	Val
	27	tct	ccg	ccg	gtt	Ser	Pro	Arg	Val
	29	acg	cct	ccg	ggt	Thr	Pro	Arg	Gly
	30	ct	tag	tgg	tgg	Pro	Stop	Trp	Trp

Activity of Fab clones containing 2 TPO mimetic peptides

Fig. 10



F: S. 11

Activity of Fab clones containing 2 or 3 TPO mimetic peptides

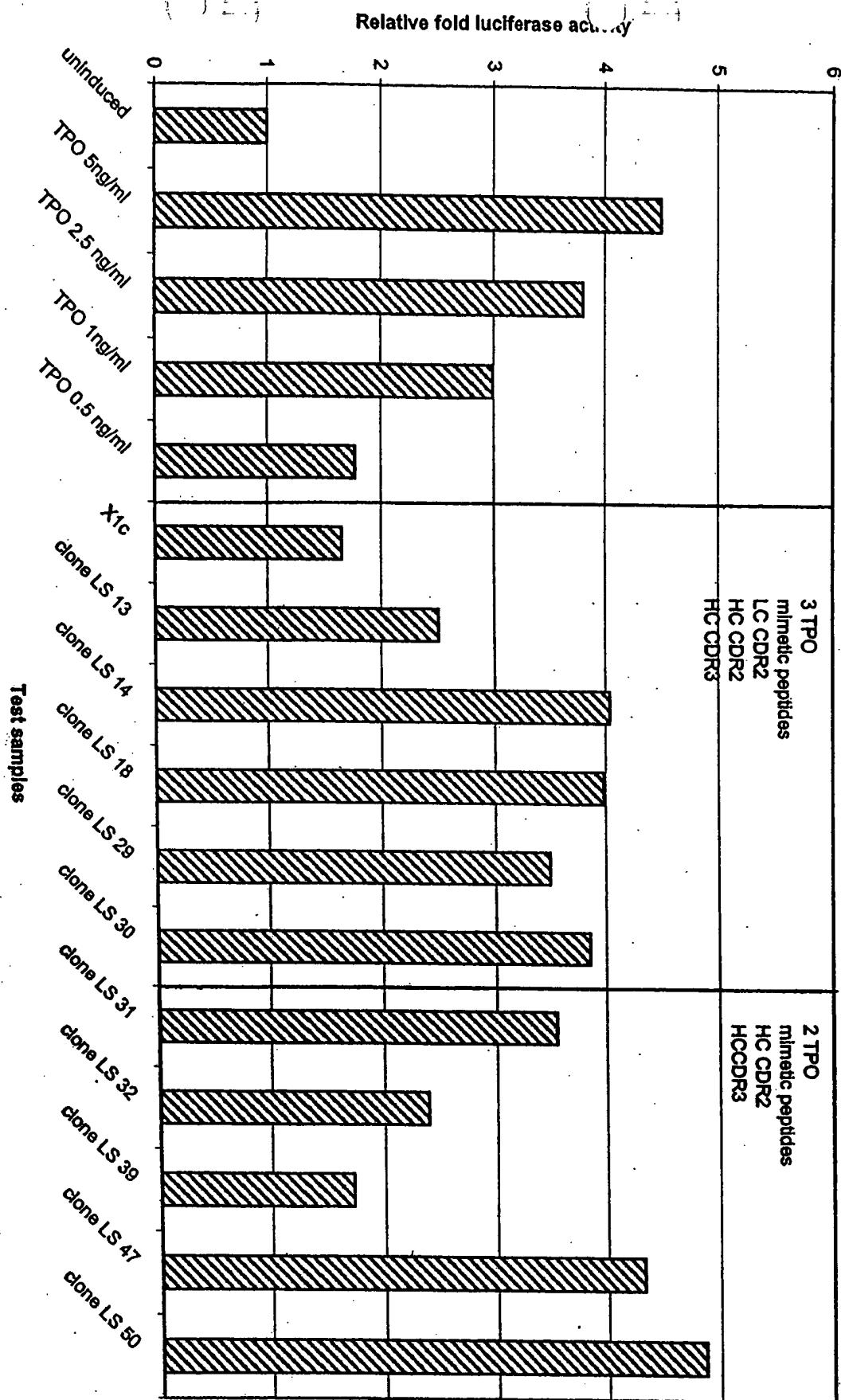
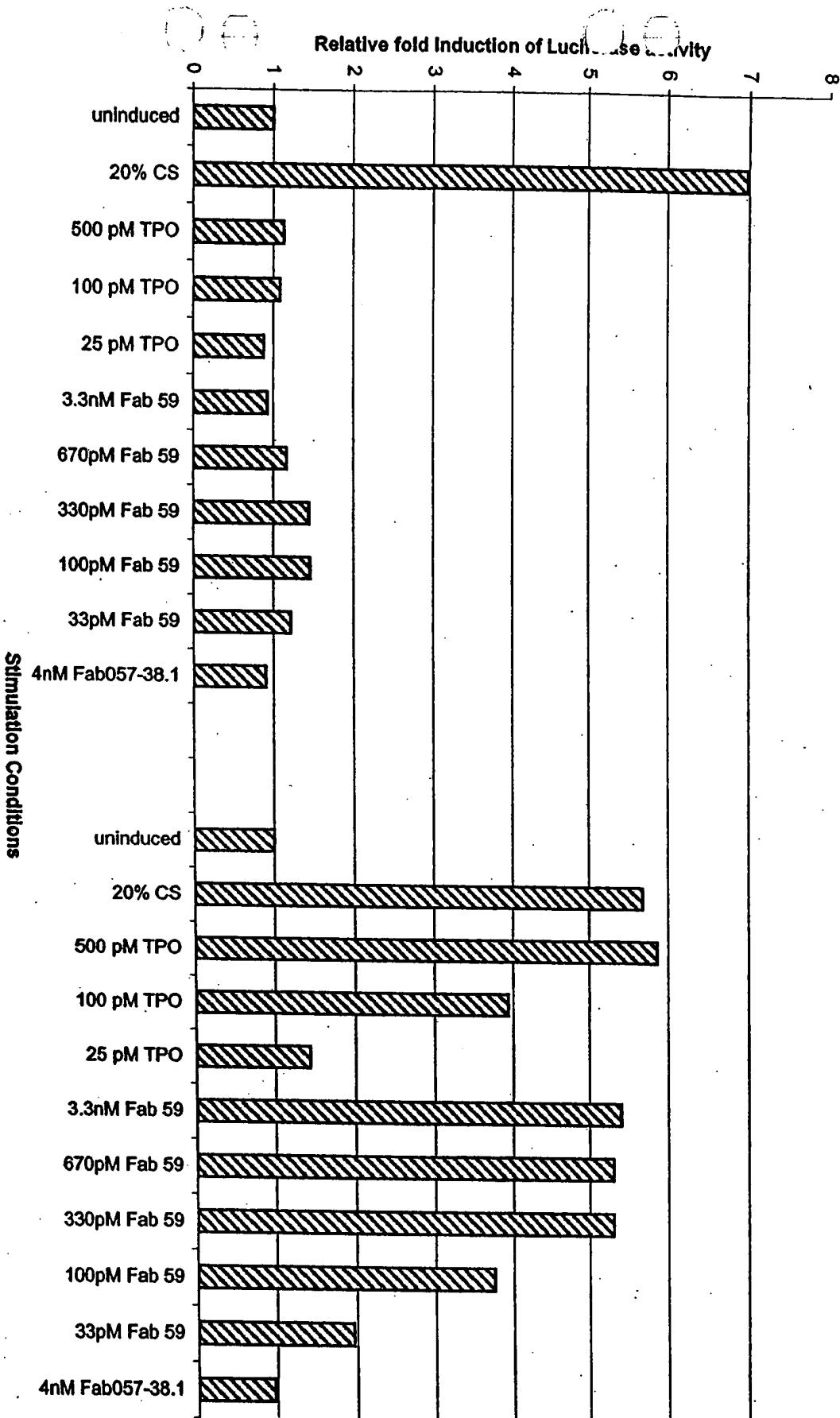


Fig. 12

TPO mimetic Activity of semi-purified Fab clone 59



(SEQ ID NO: 67)

SG1.1 - TPO Heavy Chain (Bold denotes TPO mimetic) Amino acid sequence:

MKIWSWVIL**F**LLSVTAGVHSQVQLVQSGAEVKPGASVKVSCKASGYIFSNYWIQW
VRQAPGQGLEWMGEILPGSGSTEY**T**ENFKDRVTMTRDTST**T**Y**M**ELSSLRSED
TAVYYCARLPIEGPTL**R**QWLAARAPVWGQGTLVTVSSASTKGPSV**P**LAPCSR
STSESTAALGCLVKDYF**P**EPVTVWSN**S**GALTSGVHTFP**A**VLQSSGLYSLSSVTV
PSSNFGTQTYTC**N**VDHKPSNTKV**D**KTVERKCCVE**C**PPCPAPPVAGPSV**F**LFPPKP
KD**T**LMSRTP**E**TCVV**V**DVS**Q**EDPEVQFNWYD**V**E**H**NA**K**TP**R**EEQFN**S**TY
RVVSVLTVL**H**QDWLN**G**KEY**K**CKVSNKGLPSSIE**K**TI**S**AK**G**Q**P**REP**Q**Y**V**TL**P**PSQ
EEMTKNQV**S**LTCLV**K**GFYPSDIA**V**E**W**ES**N**GQ**P**ENNY**K**TPP**V**L**D**SD**G**SFF**L**Y**S**R
TVD**K**SRW**Q**EG**N**V**F**SCS**V**M**H**EA**L**HN**Y**T**Q**KS**L**SL**G**K.

(SEQ ID NO: 68)

SG1.1 - TPO Heavy Chain (Bold denotes TPO mimetic) Nucleic acid sequence:

ATGAAGTGGAGCTGGG**T**ATTCTCT**C**CTGT**C**AGTA**A**CTGCCGGCG**T**CCA
CTCCC**A**GT**C**CA**A**CTGG**T**GA**A**TC**C**GG**C**CC**G**AG**G**T**C**AA**G**A**A**GCC**A**GGGG**G**
TCAG**T**CAA**A**GT**T**GT**C**CT**G**TAA**A**AG**C**TAG**C**GG**C**T**A**T**A**TT**T**TT**T**CT**A**ATT**A**TT**T**GG**A**T
TCA**A**TGG**G**GT**C**GT**C**AG**G**CCCC**GG**GC**AG**GG**C**CT**G**GA**A**T**G**GA**T**GG**G**GT**G**AG**A**TC
TTAC**C**GG**G**CT**C**GG**T**AG**C**ACC**G**A**A**T**A**CC**G**AA**A**TT**T**AA**A**GC**C**GT**G**TT**A**
CT**A**T**G**AC**G**CG**T**GA**C**AC**A**CT**T**CG**A**CT**A**GT**A**CG**T**AT**A**CA**T**GG**A**GT**C**T**C**CC**A**GG**C**CT**G**
CG**A**T**C**GG**A**GG**A**CA**C**GG**C**GT**C**T**A**TT**A**TT**G**CG**C**GC**T**TT**G**CCA**A**TT**G**A**AG**GG
CC**G**AC**G**CT**G**GG**C**AA**T**GG**C**T**G**GC**G**CG**C**GC**T**GT**T**TT**G**GG**G**TC**A**AG
GA**A**CC**C**T**GG****T**CA**C**GT**T**CT**G**AG**G**CG**C**CT**C**CC**A**CC**G**CC**C**AT**C**CG**T**CT**C**CC**C**
CT**G**GG**C**CC**C**CT**G**CT**C**CC**A**GG**G**AG**A**GC**A**CG**C**CC**C**CT**G**GG**C**CT**G**
TGG**T**CA**AG**GA**T**ACT**T**CCC**G**AA**C**GG**T**GA**C**GG**T**GT**C**GT**G**GA**A**CT**C**AG**C**GC**C**
C**C**T**G**AC**A**CG**G**GG**C**GT**G**CA**C**AC**A**CT**T**CC**GG**CT**G**TC**T**AC**A**GT**C**CT**C**AG**G**ACT**T**
A**C**T**C**CT**C**AG**C**AG**G**GT**G**GA**C**CG**C**GT**C**CC**A**CT**T**CG**C**AC**C**CC**C**AG**A**C
CT**A**CA**C**CT**G**CA**A**CG**T**AG**A**T**C**ACA**A**GC**C**CC**A**AC**A**CC**A**AG**G**T**G**GA**C**AC**A**AG**A**C
A**G**T**T**GA**G**CG**C**AA**A**AT**G**T**T**GT**C**AG**G**AT**G**CC**C**AC**C**GT**G**CC**A**GG**G**AC**A**CT**T**GT
G**C**AG**G**AC**C**GT**C**AG**T**CT**C**CT**T**CC**CC**AAA**A**CC**A**AG**G**AC**A**CC**C**TC**A**GT**G**AT
CT**CC**CG**G**AC**C**CC**C**GT**G**AG**G**T**C**AC**G**GT**C**GG**C**TC**A**GG**G**AT**C**AA**A**GT**G**CA**A**
CC**C**CG**A**GG**T**CC**A**CT**G**GT**C**AC**T**GG**A**GT**C**GG**T**GT**C**GG**G**AG**G**T**C**ATA**A**TC**G**CA**A**
AG**A**CA**A**AG**C**CG**C**GG**G**AG**G**AC**G**CAG**T**GT**C**AC**A**CC**C**CT**G**CC**C**CC**A**TC**C**CC**G**
T**C**CT**C**AC**C**GT**C**CT**G**AC**C**AG**G**ACT**G**GT**C**GA**C**GG**C**AA**G**GA**T**CA**A**AG**G**T**C**AA**A**GT**G**CA**A**
GG**T**CT**C**CA**A**AA**A**GG**C**CT**C**CC**G**T**C**TC**C**AT**G**AG**A**AA**A**CC**A**TC**C**CA**A**AG**G**
AA**A**GG**G**CA**G**CC**C**GA**G**AG**G**AC**G**CA**C**AG**G**GT**C**AC**A**CC**C**CT**G**CC**C**CC**A**TC**C**CC**G**
G**G**AT**G**AC**A**AA**A**AC**C**AG**G**GT**C**AG**G**CT**C**AC**T**GG**A**GT**C**CC**C**CT**G**TC**A**AG**G**C**T**CT**A**
CC**A**CG**C**AC**A**TC**G**CC**G**T**G**AG**G**AT**G**GG**A**GA**G**CA**A**TC**G**GG**A**GA**A**CA**A**CT
A**C**AA**A**GA**C**AC**G**CC**C**CT**C**CC**G**T**G**GT**C**GG**A**CT**C**CC**C**CT**G**TC**T**CT**C**TC**A**GT**G**
AG**G**CT**A**AC**C**GT**G**GA**A**AG**A**GC**A**GG**G**GT**C**AG**G**AG**G**GG**G**GA**A**AT**G**T**C**TC**T**CT**C**AT**G**T
CC**G**T**G**AT**G**CA**T**GA**G**GG**C**T**C**TC**G**CA**A**CC**A**CT**A**CA**C**AC**A**CA**G**AG**G**CC**C**CT**C**CC**C**
GT**C**CT**G**GT**G**AA**A**AT**G**

Fig. 13A

(SEQ ID NO: 69)

SG1.1 Light Chain Amino Acid Sequence

→ *MDMRVPAQLLGLLLWLRGARCDIQMTQSPSSLSASVGDRVITCGASENIYGALN*
WYQQKPGKAPKLLIYGATNLADGVPSRFSGSQGTDFTLTISLQPEDFATYYCQ
NVLNTPLTFQGQTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNFYPREAK
VQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTSKADYEKHKVYACEVTH
QGLSSPVTKSFNRGEC.

(SEQ ID NO: 70)

SG1.1 Light Chain Nucleic Acid Sequence

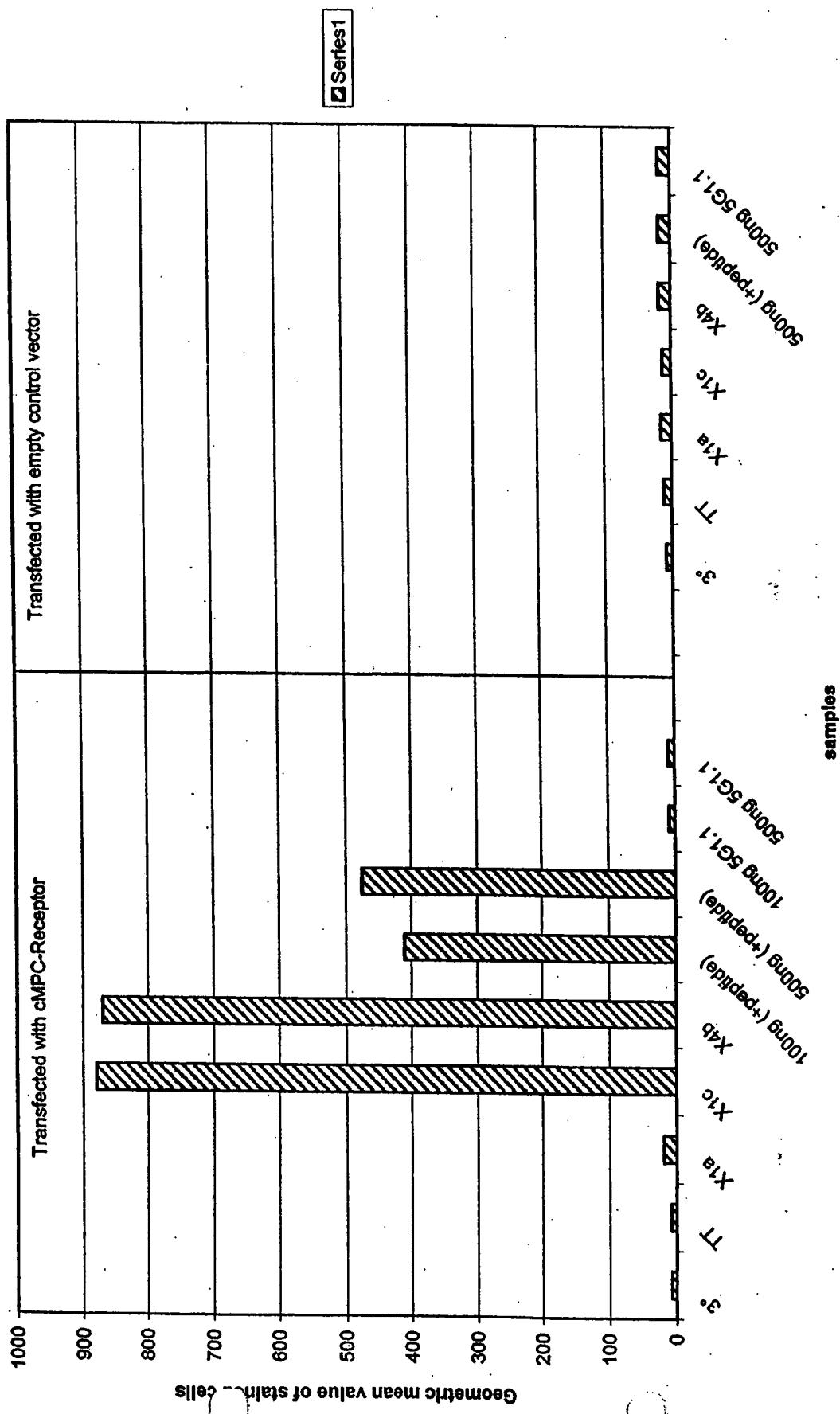
→ *ATGGACATGAGGGTCCCCGCTCAGCTCTGGGGCTCTGCTACTCTGGCTCCG*
AGGTGCCAGATGTGATATCCAGATGACCCAGTCCCCGCTCCCTGTCCGCCT
CTGTGGCGATAAGGGTCAACCATCACCTGCGCGCCAGCGAAAACATCTATGG
CGCGCTGAACCTGGTATCAACAGAAACCCGGAAAGCTCCGAAGCTTCTGATT
TACGGTGCACGAACCTGGCAGATGGAGTCCCTCTCGCTTCTCTGGATCCGG
CTCCGGAACGGATTCACTCTGACCATCAGCAGTCTGCAGCCTGAAGACTTC
GCTACGTATTACTGTCAGAACGTTAAATACTCCGTTGACTTTGGACAGAGGG
TACCAAGGTGGAAATAAAACGAACGTGGCTGCACCCTGTCTCATCTTCC
CGCCATCTGATGAGCAGTGAATCTGGAACCTGCCCTGTGTGCCCTGCTG
AATAACTCTATCCCAGAGAGGGCAAAGTACAGTGGAAAGGTGGATAACGCC
TCCAATCGGGTAACCTCCAGGGAGAGTGTACAGAGCAGGACAGCAAGGACA
GCACCTACAGCCTCAGCAGCACCTGACGCTGAGCAAAGCAGACTACGAGA
AACACAAAGTCTACGCCCTGCGAAGTCACCCATCAGGGCTGAGCTCGCCCGT
CACAAAGAGCTCAACAGGGAGAGTGTAG

Note: Italics denotes leader sequence

Fig. 13B

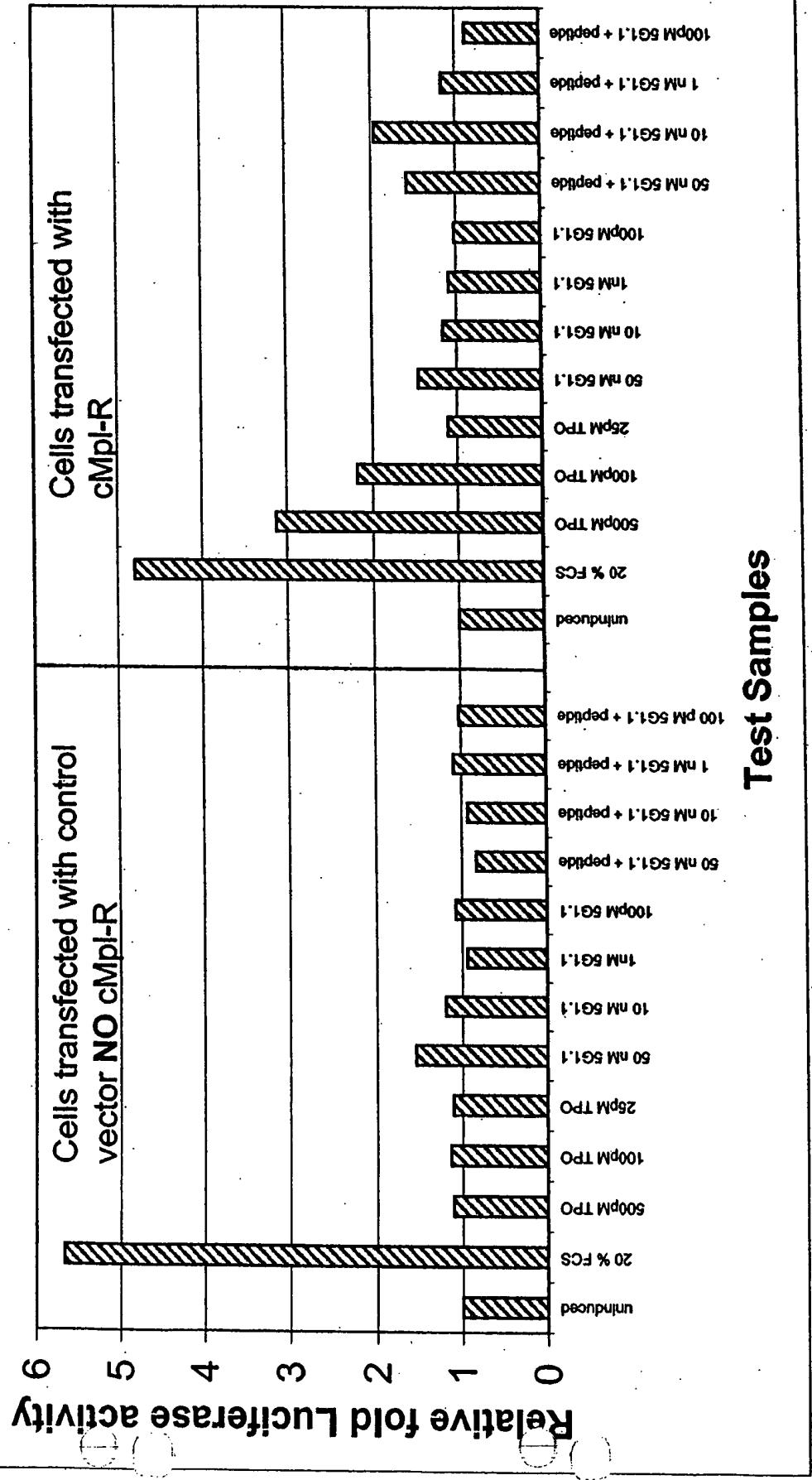
Fig. 14

FACS staining on transfected 293 cells



5. 5

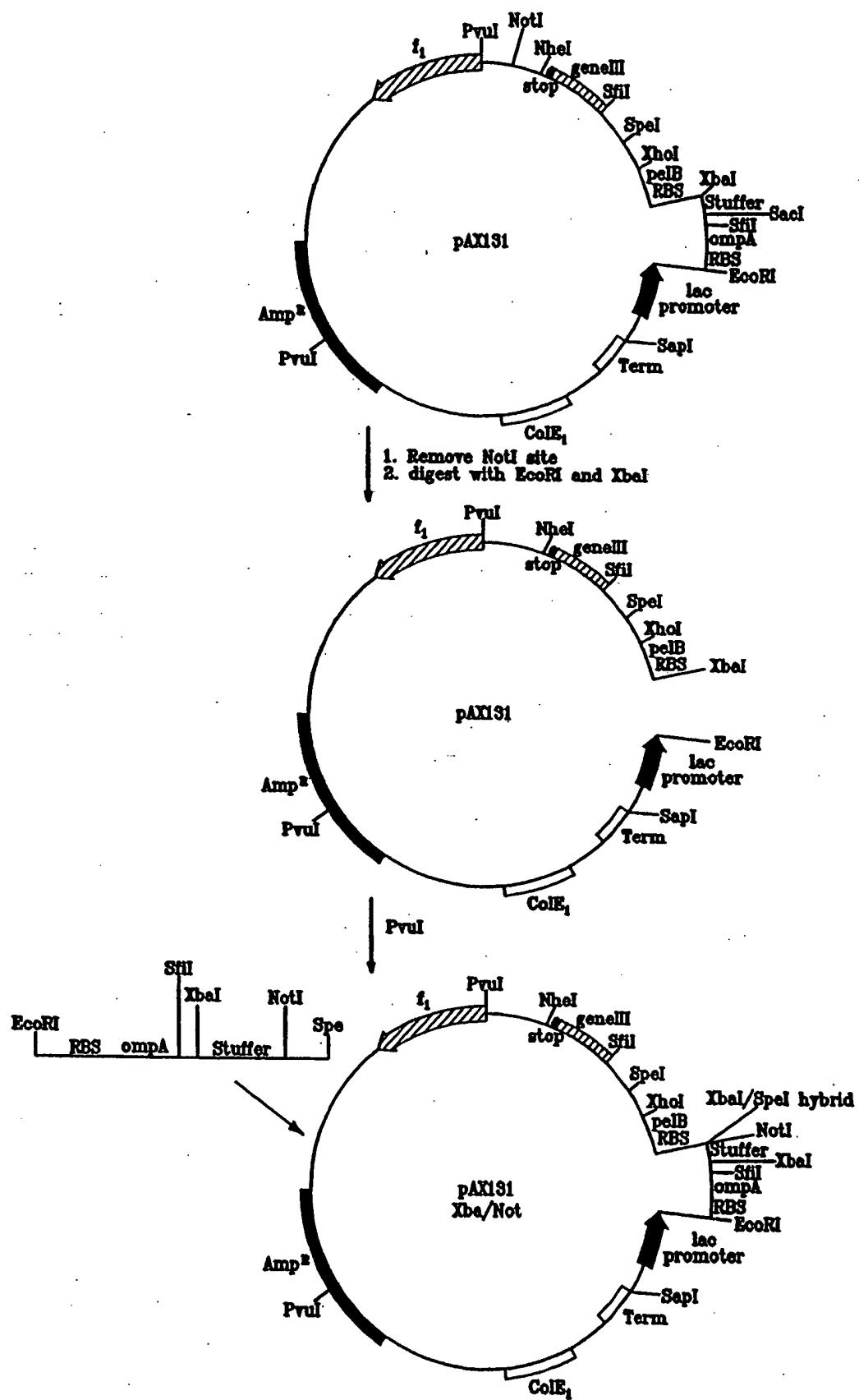
Activity of 5G1.1 containing the TPO mimetic Peptide



WATERFALL REGION OF 4-29 LIGHT CHAIN

86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107
TAT	TAC	TGC	CAA	CAG	TAT	AAT	AGT	TAC	CCT	CCC	ACT	TTC	GCG	CCT	GGG	ACC	AAA	GTG	GAT	ATC	AAA

Fig. 16



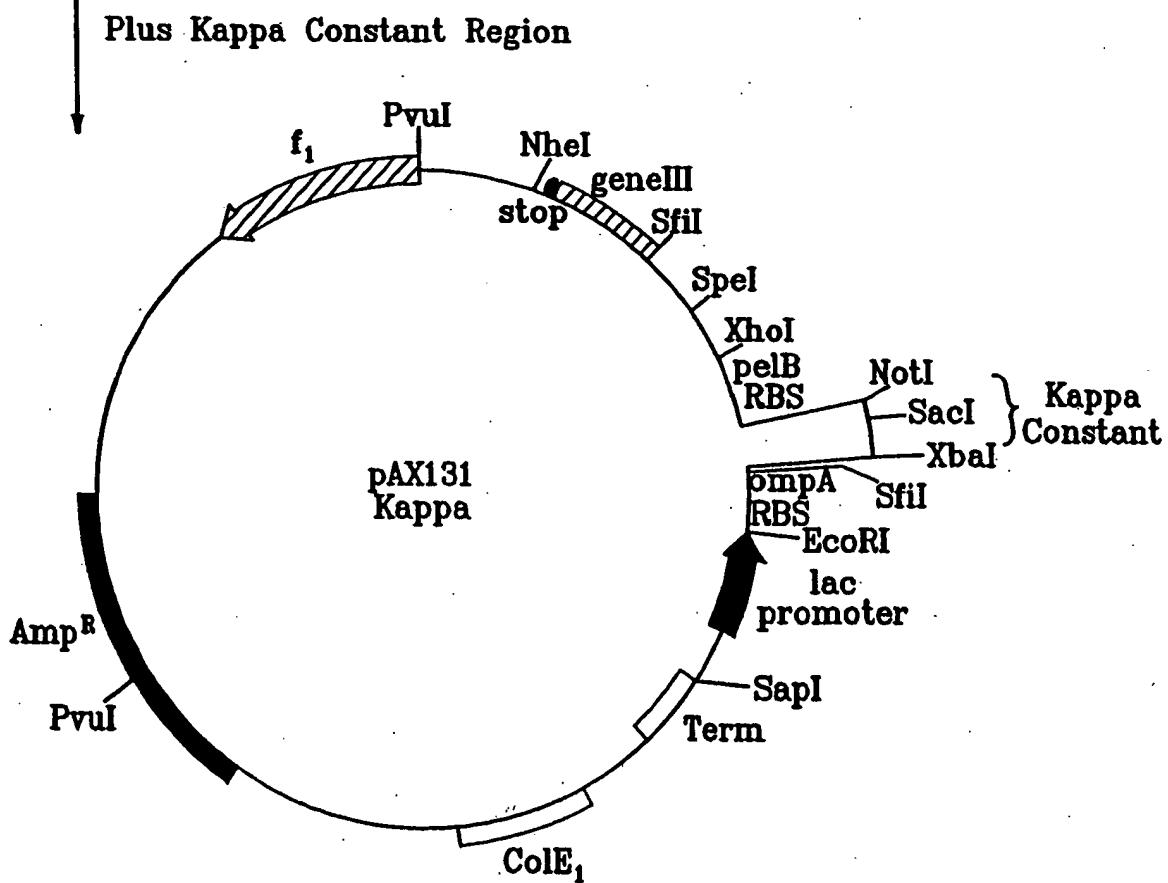
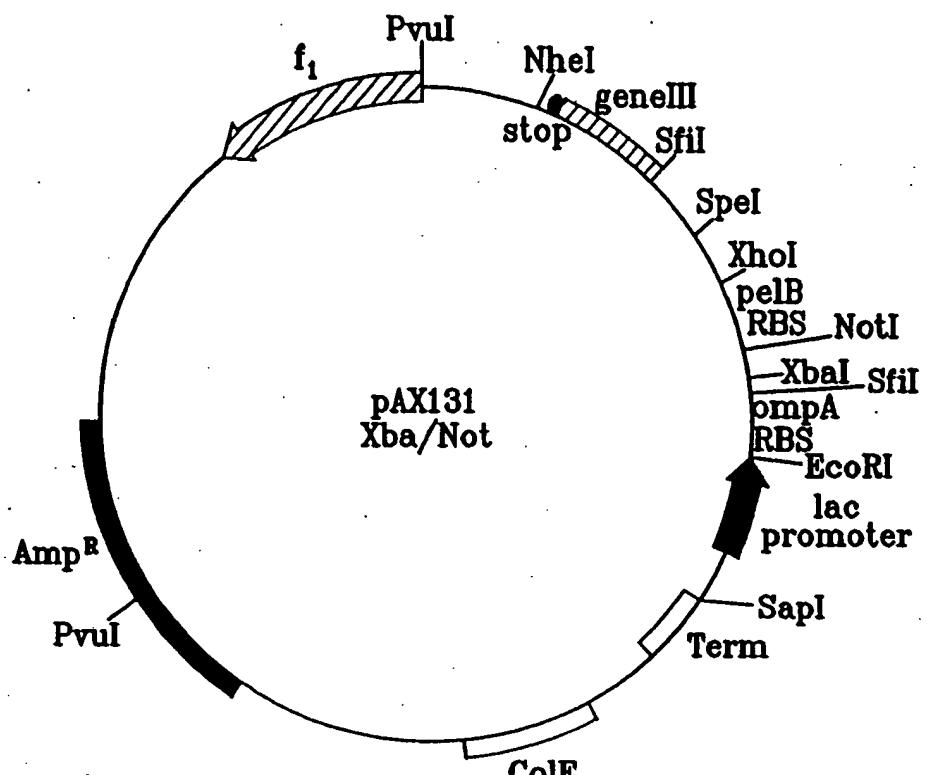


FIG. 18

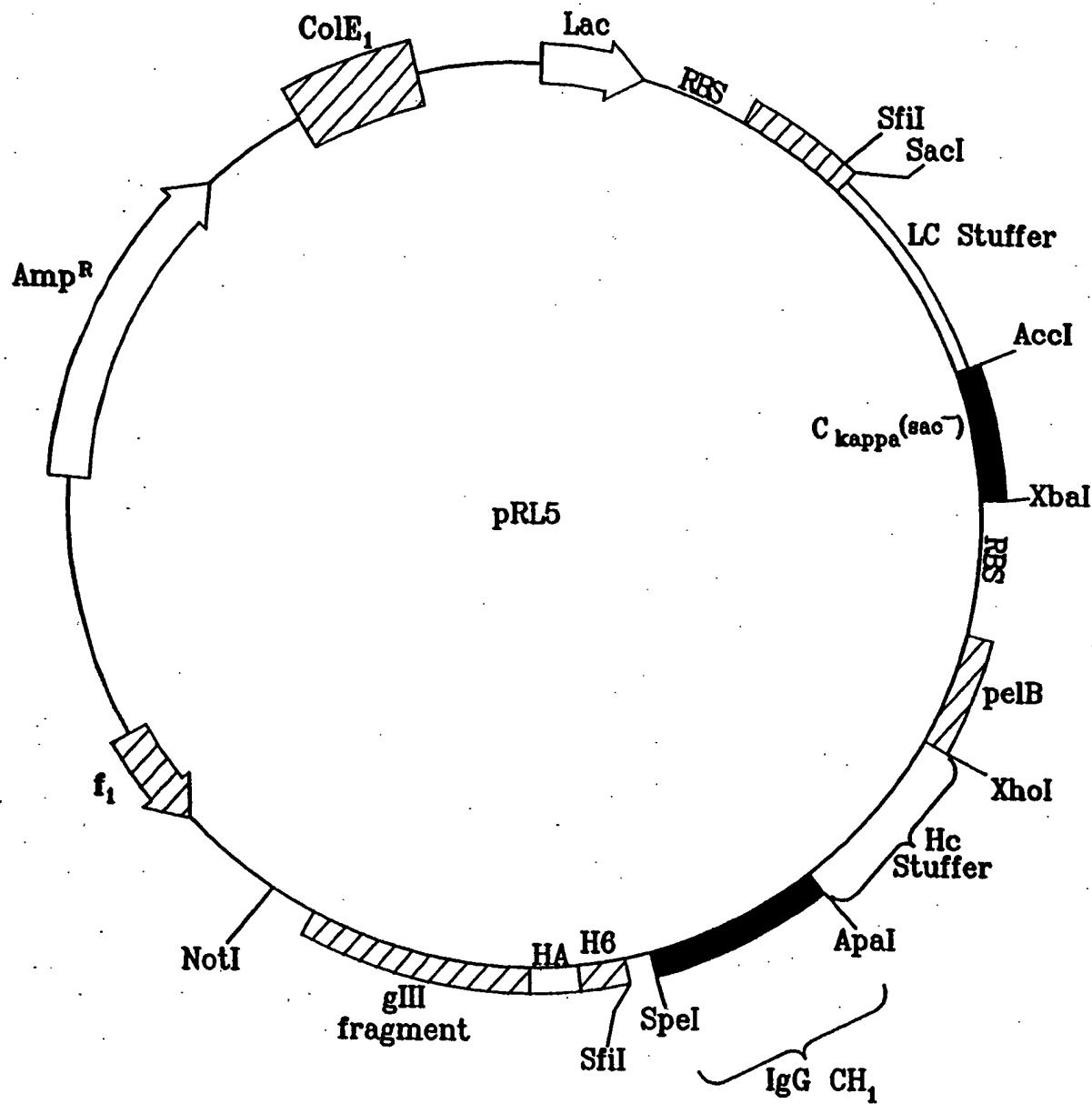
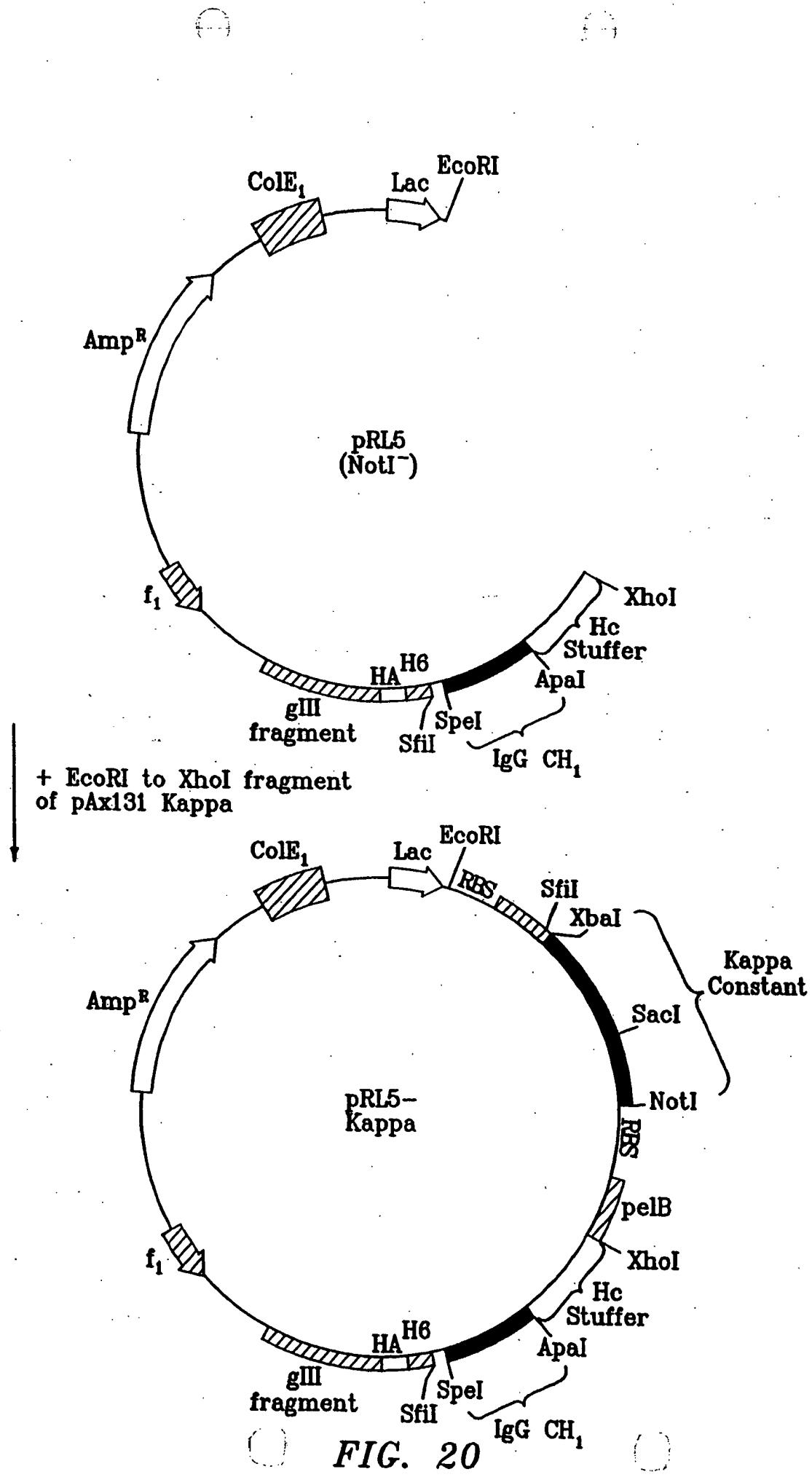


FIG. 19



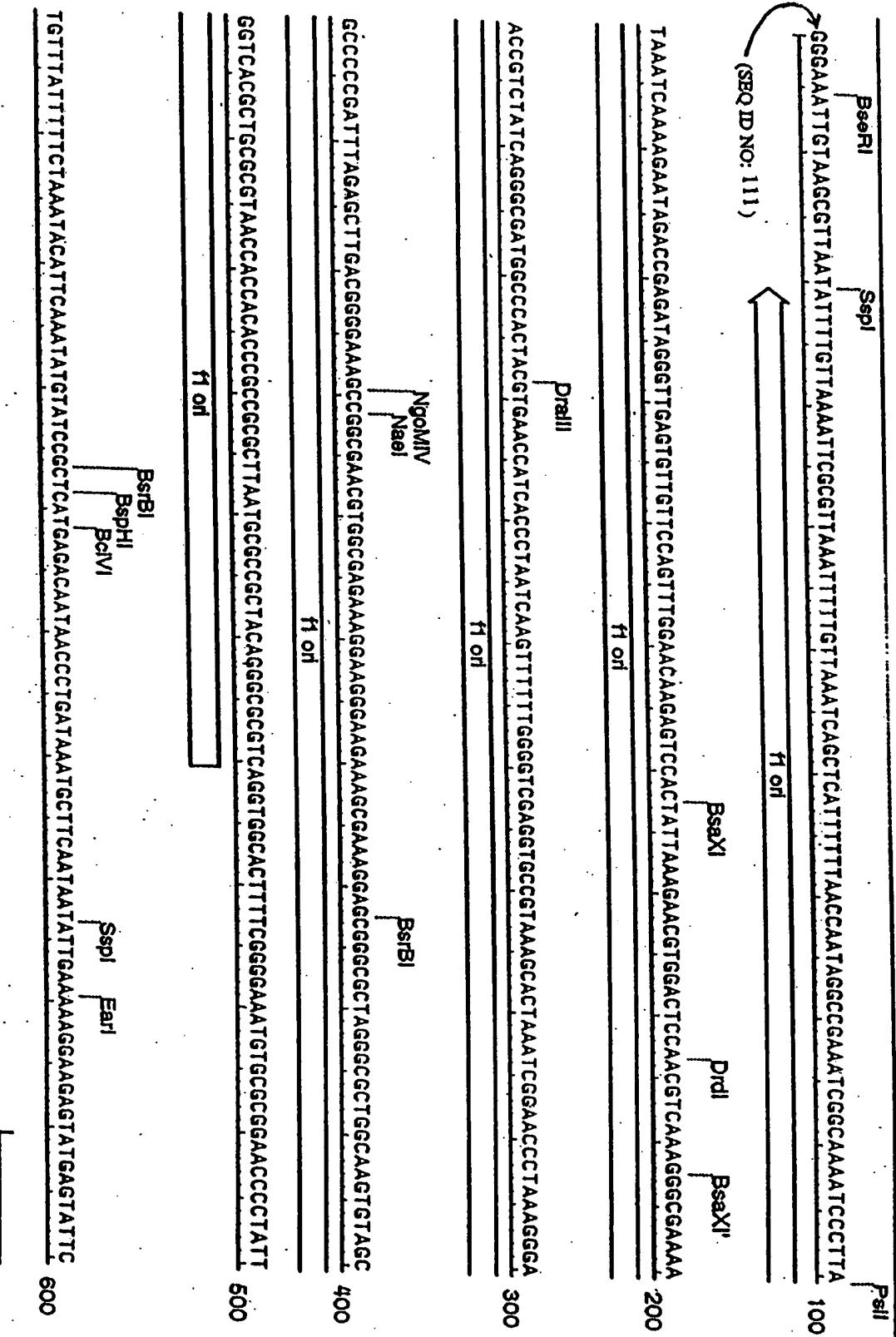


Fig. 21A

AACATTCCGTGTCGCCCTATTCCCTTTGGCCATTGGCCTCTGTTGCTACCCAGAACGCTGGTGAAGTAAAGATGCTGAAGATCA 700

— beta-lactamase —

ApalI
BssH I
Eco57I

AclI
XmnI

PstI

GTTGGGTGCACGAGTGGGTTACATCGAACTGGATCTCAACAGGGTAAGATCCTGAGAGTTGGGGGAAGAACGTTTCCAAATGATGAGCACTTTT 800

— beta-lactamase —

BcgI'

BcgI

Scal

AAAGTCTGCTATGTTGGGGTATTATCCCGTATGACGGGGCAAGAGCAACTCGGTGCCCATACACTATCTCAGAATGACTTGGTTGAGTCT 900

— beta-lactamase —

BstI

BstI

CACCAAGTCACAGAAAGCATTTACGGATGGCATGGACAGTAAGAGAATTATGCAGTGCTGCCATAACCATGAGGTATAACACTGGGCCAACTTACTCTT 1000

— beta-lactamase —

PvuI

GACAACGGATGGGGACCGAAGGGAGCTAACCGCTTTTGCACAAACATGGGGATCATGTAACTCGCCTTGATCGTTGGAACCGGAGCTGAATGAAAC 1100

— beta-lactamase —

Fig. 21B

Fig. 21D

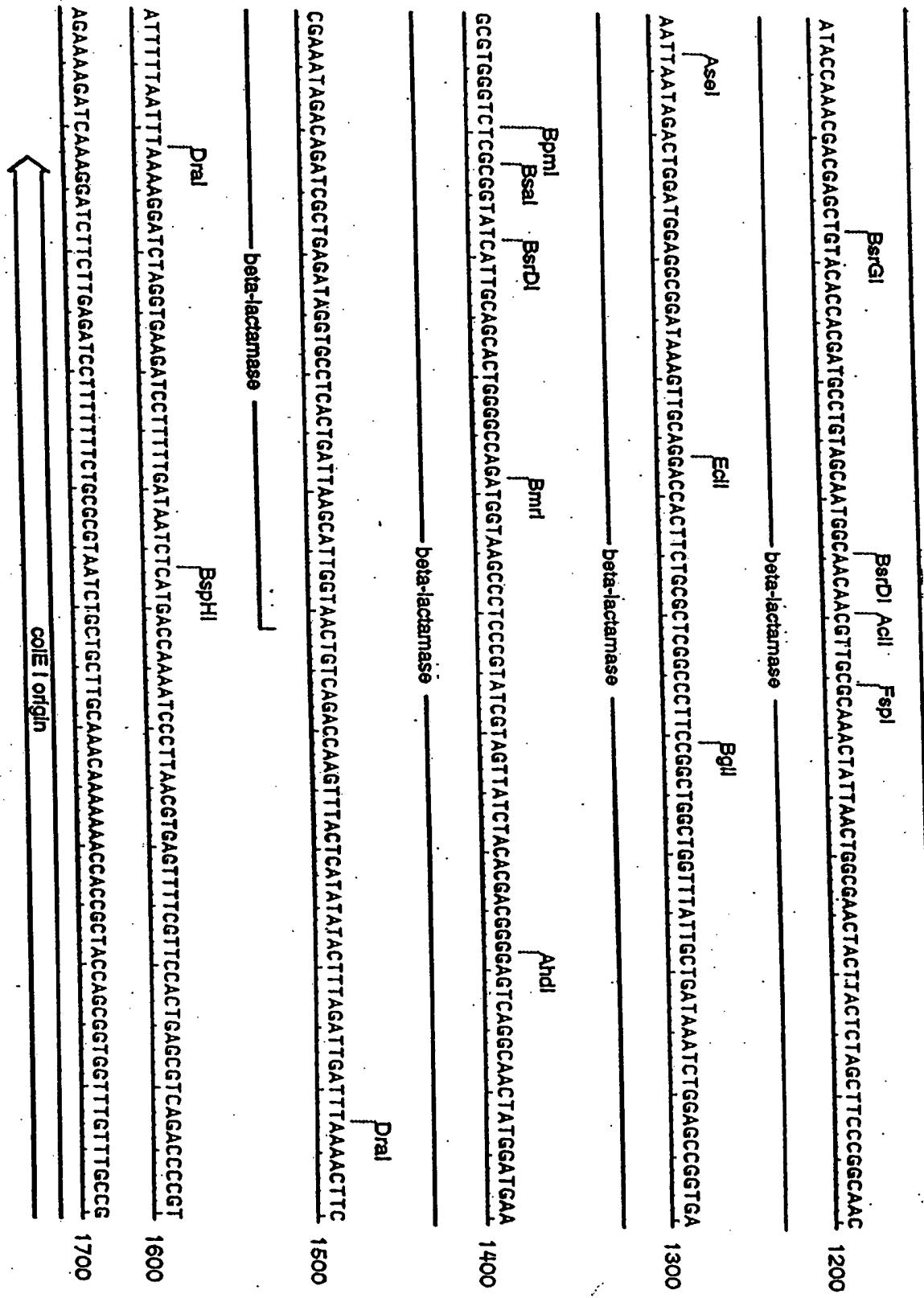


Fig. 21E

Eco571
GATCAAGAGCTACCAACTTTTCCGAAGCTAACTGCTTCAGCAGAGCGCAGATACCAAATACTGCTCTAATGCTAGGCCACCACT 1800
coIE I origin

AlwNI
TCAAGAACTCTGTAGCCACCGCCTACATACCCACTCTGCTAATCCCTGTTACCACTGGCTGCTGCCAGTGGCAATAGCTGCTTACCGGCTTGGACTC 1900
coIE I origin

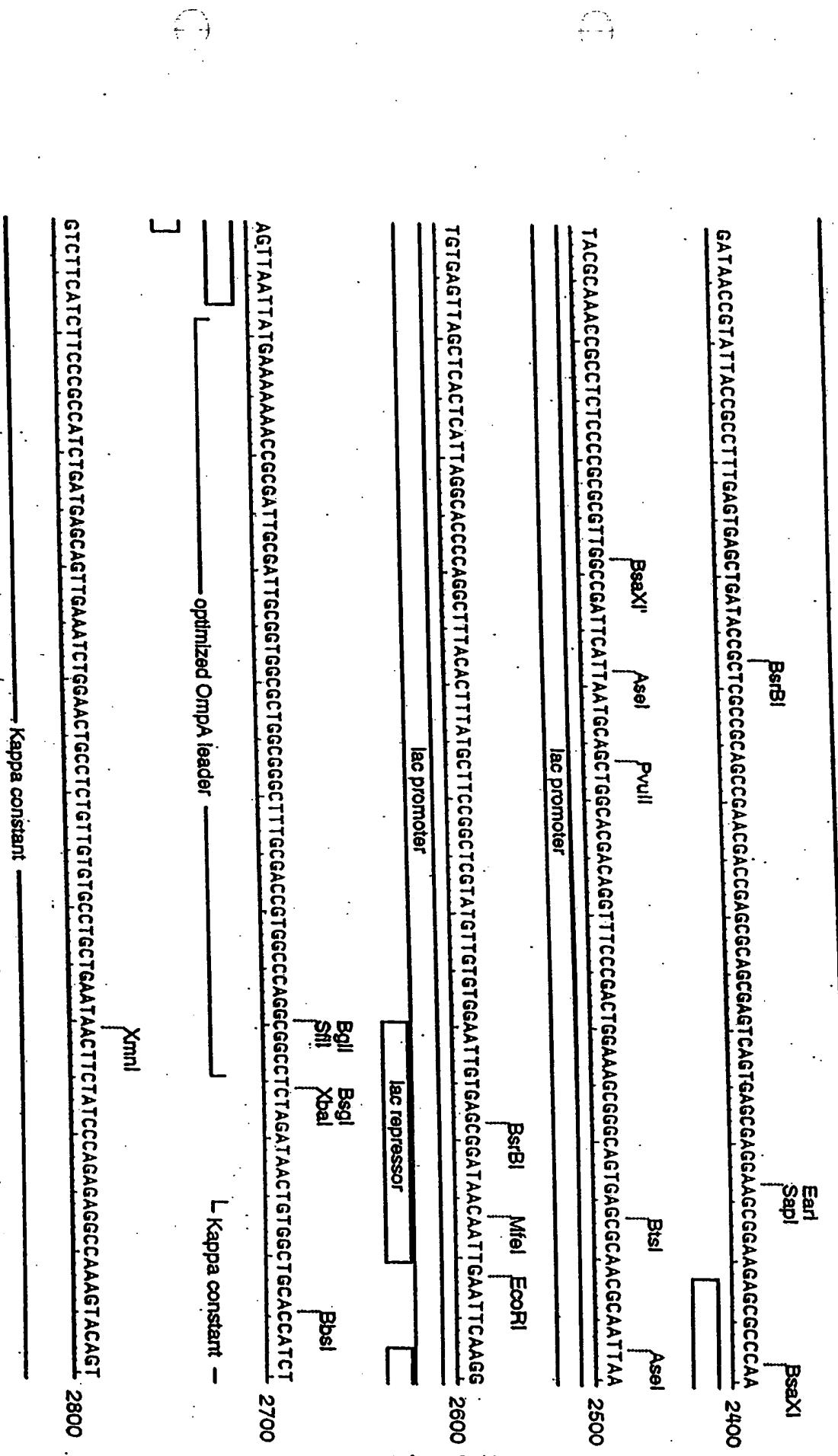
ApalI
AAGACGATAGTTACCGATAAGGCCAGCGGTGGCTGAACGGGGTTCGTGCACACAGCCCAGCTGGAGCGAACGACCTACACCGAACTGAGATAC 2000
coIE I origin

BclI **BcVI**
C7ACAGCGCTGAGCTATGAGAAAGGCCACCGCTCCGAAGGGAGAAAGGGGGACAGGTATCCGGTAAGGGCAGGGTGGAACAGGAGAGCCACGGG 2100
coIE I origin

PstI
AGCTTCCAGGGGAACGCCCTGGTATCTTATAGCTCTGGGTTTGCACCTCTGACTTGAGCGCTGATTTGTGATGCTCTCAGGGGGCGGAG 2200
coIE I origin

PstI
CCTATGGAAAAACGCCAGCAACGCCACCTTACGGTCTGGCTTGTGCTCACATGTTCTGCTTATCCCCTGATTCTGTG 2300
coIE I origin

Fig. 21F



GTCTTCATCTTCCCCATCTGATGAGGAGTTGAATCTGGAACCTGCCTCTGCTGCTGCTGATAACTTCTATCCAGAGAGGCCAAAGTACAGT 2800

GGAGGTGGATAACGCCCTCCAACTGGGTAACTCCCAGGAGACTGTCAACAGAGCAGGACAGCAAGGCACCTACAGCCAGCAGCACCTGACGCT BbvCI Bpu10I Bpl 2900

- Kappa constant

AlwNI
Bpu10I
EcoICRI

CAGCAAAGAGACTACGGAGAACACAAAGCTACGCCCTGCCAACCTCAGGGCCTGAGCTCGCCCTCACAAAGAGCTCAACAGGGAGAGT 3000

- Kappa constant

BCI

NGOMA
Nael

TAAGCGGCCACTAGATAATTAGGAGATAATTGAAATACTGCTGCCGACCCGGGGCTGCTGCTGGCGGCAGCCGGCATGG 3100

L

18

Fig. 21G

MC 50116

ECORY

TCGAGCTTCGTGCCCTAGAGTGCCTCACAGCAGCTCCGGGATATCACCGTGTATCCACATCCAATGAAGTAGTGCTCTAGACCCCC
3300

HC stuffer

Fig. 21G

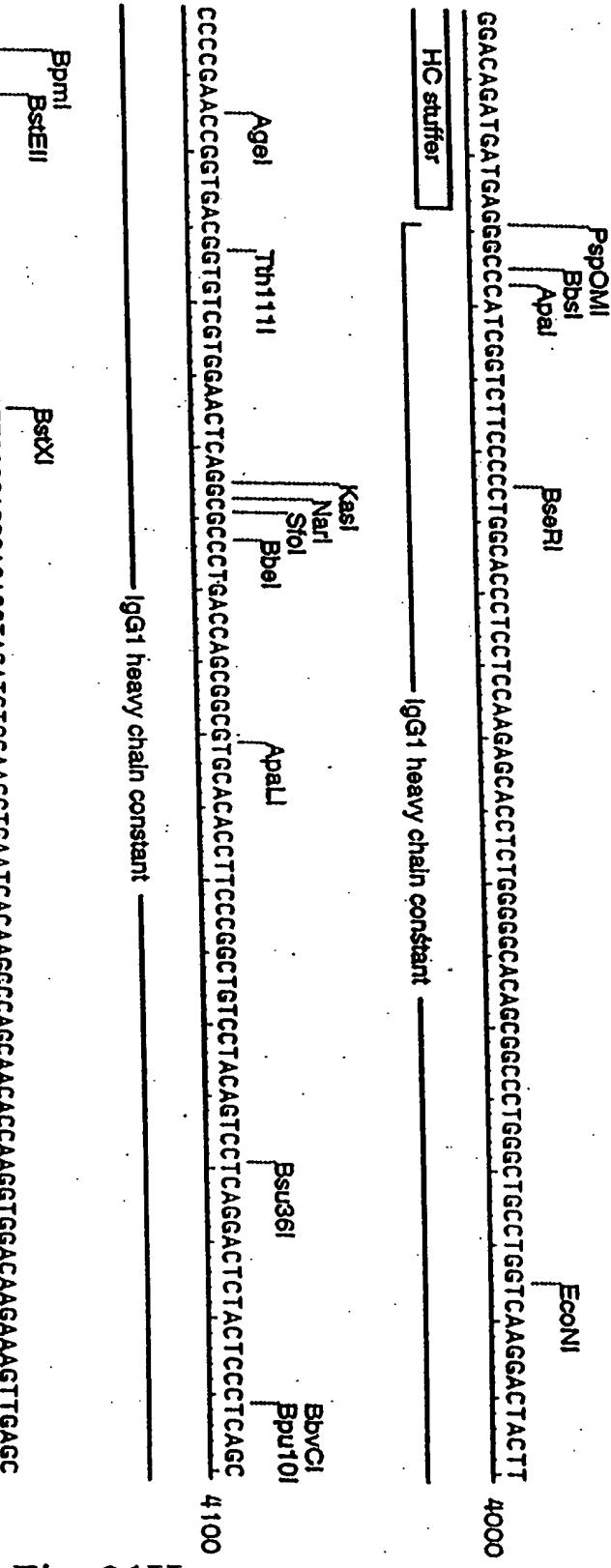
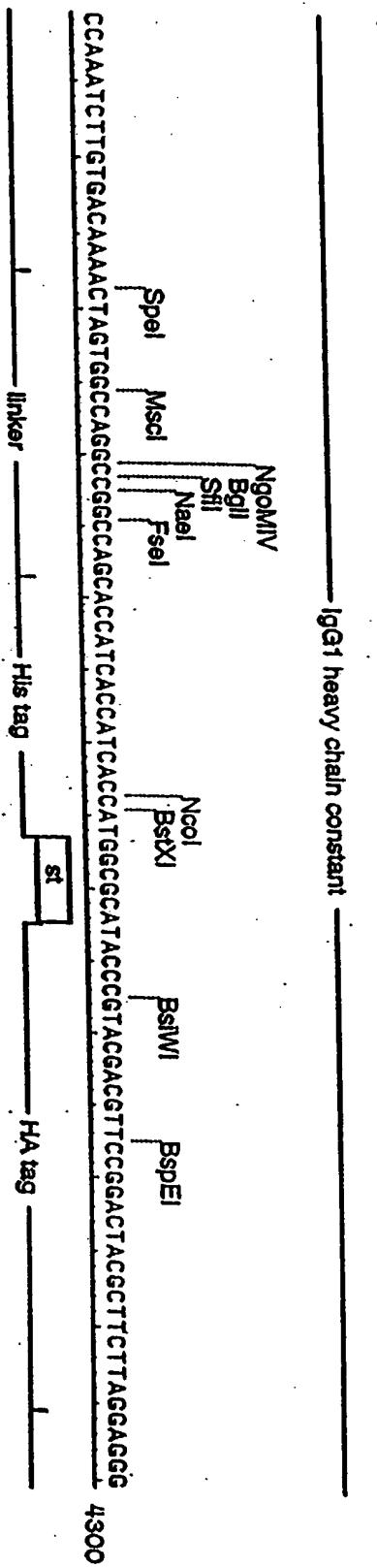


Fig. 21H



TGGGGCTCTAGGGGGCTCTGGGGCTCTGGGGGGCTCTGGGGCTCTGGGGGATTTGATTATGAAAAGATGGCA 4400

AACGCTAATAAGGGGCTATGACCGAAATGCCATGAAACCGCCTACAGTCTGACGCTAAAGGCAAACCTGATTCTGCGCTACTGATTACGGCTG 4500

gene III

gene III

ClaI

CTATCGATGGTTCATGGTACGGTTCCGGCCTGCTAATGGTAATGGTCTACTGGTGTGATTGCTGGCTCTAATTCCAAATGGCTCAAAGTCGGTA 4600

gene III

BsaXI'

CGGTGATAATTACCTTAATGAATAATTCCGTCATATTACCTTCCCTCCCTCAATCGGTTGAATGTCGCCCTTGTCTTASCCCTGGTAACCA 4700

gene III

TATGAATTCTATTGATTGACAATAACTTATCCGGGGTCTTGCCTTCTTATATGTTGCCACCTTATGATGATTTCACGTTG 4800

gene III

EagI

NgoMIV

EagI

NaeI

Asel

XbaI
BsaXI
SspI

4883

Fig. 211

Figure 22

VH: L22582 (human germline family member VH1-69)

GCAGGATTAGGGCTGGTCTCTCAGCATCCCACACTGTACAGCTGATGTGGCATCTG
TGTTTCCTTCATCGTAGATCAGGCTTGAGCTGTGAAATACCCCTGCCTCATGCATATGCA
AATAACCTGAGGTCTCTGAGATAAATATAGATATATTGGTGCCTGAGAGCATCACATAA
CAACCACATCCTCTAAAGAAGGCCCTGGGAGCACAGCTCATCACCATGGACTGGACC
TGGAGGTTCTCTTGTGGCAGCGCTACAGGTAAAGGGCTTCCTAGTCCTAAGGCTGAG
GAAGGGATCCTGGTTAGTAAAGAGGATTTATTCAACCCCTGTGTCTCTCCACAGGTGTC
CAGTCCCAGGTGCAGCTGGTGCAGTCTGGGCTGAGGTGAAGAAGCCTGGGTCTCGGTGA
AGGTCTCTGCAAGGCTCTGGAGGCACCTTCAGCAGCTATGCTATCAGCTGGGTGCGACA
GGCCCTGGACAAGGGCTTGAGTGGATGGAGGGATCATCCCTATCTTGGTACAGCAAAC
TACGCACAGAAGTCCAGGGCAGAGTCACGATTACCGCGAACGAATCCACGAGCACAGCCT
ACATGGAGCTGAGCAGCCTGAGATCTGAGGACACGGCCGTGTATTACTGTGCGAGAGACAC
AGTGTGAAAACCCACATCCTGAGAGTGTCAAGAAACCTGAGGGAGAAGGCAGCTGTGCG
GGCTGAGGAGATGACAGGGTTATTAGGTTAAGGCTGTTACAAATGGGTTATATATTG
AGAAAAAAAGAACAGTAGAAACAAGTACATACTCCTCTAATTAAAGATAATTATTCCATT
CAAGAGTCGTAATAT (SEQ ID No. 153)

JH---JH6

H3

CDR3

100

110

JH6 YYYYYGMDVWGQGTTTVSS (SEQ ID No 154)

Figure 23

Vk: X12686 (human germline family member VKIII -A27)

CAGCTGCTTGCATGTCCCTCCCAGCCGCCCTGCAGTCCAGAGCCCATATCAATGCCTGG
GTCAGAGCTCTGGAGAAGAGCTGCTCAGTTAGGACCCAGAGGGAAACCATGGAAACCCAG
CGCAGCTCTCTCCTCCTGCTACTCTGGCTCCAGGTGAGGGGAACATGGGATGGTTTGC
ATGTCAGTAAAACCCCTCTCAAGTCCTGTTACCTGGCAACTCTGCTCAGTCAATACAATAAT
TAAAGCTCAATATAAAGCAATAATTCTGGCTCTTCTGGGAAGACAATGGGTTGATTAGAT
TACATGGGTGACTTTCTGTTATTCCAATCTCAGATACCACCGGAGAAATTGTGTTGAC
GCAGTCTCCAGGCACCCCTGTCTTGTCTCCAGGGAAAGAGCCACCCCTCCTGCAGGGCCA
GTCAGAGTGTAGCAGCAGCTACTTAGCCTGGTACCGCAGAAACCTGGCCAGGCTCCAG
GTCCTCATCTATGGTGATCCAGCAGGGCCACTGGCATCCCAGACAGGTTCAGTGGCAGT
GGGTCTGGACAGACTCACTTCACCATCAGCAGACTGGAGCCTGAAGATTTCAGTGT
ATTACTGTCAAGCAGTATGGTAGCTCACCTCCCACAGTGATTCAAGCTTGAAACAAAAACCTCT
GCAAGACCTTCATTGTTACTAGAT TATACCAGCTG (SEQ ID NO 155)

JK

L3

CDR3

--

100

Jk1 WTFGQGTKVEIK (SEQ ID NO. 156)

Figure 24

pAXB116 Fab'-gVh

(SEQ ID NO 157) pelB leader ATG AAA TAC CTA TTG CCT ACG GCA GCC GCT GGA TTG TTA TTA CTC GCT GCC CAA
 (SEQ ID NO 158) M K Y L L P T A A A G L L L L A A Q
pelB leader
 CCA GCC ATG GCG CAG GTG CAG CTG GTG CAG AGC GGC GCG GAA GTG AAA AAA CCG
 P A M A Q V Q L V Q S G A E V K K P pAXB116 Fab'-gVh
 (SEQ ID NO 159) Q S G A E V K K P TT-Vh(CDR3-TPO)
 (SEQ ID NO 169) Q V Q L V Q S G A E V K K P L22582

CDR1-H1
 GGC AGC AGC GTG AAA GTG AGC TGC AAA GCG AGC GGC GGC ACC TTT AGC AGC TAT
 G S S V K V S C K A S G G T F S S Y pAXB116 Fab'-gVh
 G S S V K V S C R A S G G T F N N Y TT-Vh(CDR3-TPO)
 G S S V K V S C K A S G G T F S S Y L22582

GGG ATT AGC TGG GTG CGC CAG GCG CCG GGC CAG
 A I S W V R Q A P G Q G L E W M G Q pAXB116 Fab'-gVh
 A I S W V R Q A P G Q G L E W M G G TT-Vh(CDR3-TPO)
 A I S W V R Q A P G Q G L E W M G G L22582

CDR2-TPO
CTG ATT GAA GGC CCG ACC CTG CGC CAG TGG CTG GCG GCG CGC GCG AAC AGC CGC
 L I B G P T L R Q W L A A R A N S R pAXB116 Fab'-gVh
 I F P F R N T A K Y A Q H F Q G R TT-Vh(CDR3-TPO)
 I I P I F G T A N Y A Q K F Q G R L22582

GTG ACC ATT ACC GCG GAT GAA AGC ACC AGC ACC GCG TAT ATG GAA CTG AGC AGC
 V T I T A D E S T S T A Y M E L S S pAXB116 Fab'-gVh
 V T I T A D E S T G T A Y M E L S S TT-Vh(CDR3-TPO)
 V T I T A D E S T S T A Y M E L S S L22582

CTG CGC AGC GAA GAT ACC GCG GTG TAT TAT TGC GCG CGC CTG CCG ATT GAA GGC
 L R S E D T A V Y Y C A R L P I E G pAXB116 Fab'-gVh
 L R S E D T A I Y Y C A R L P I E G TT-Vh(CDR3-TPO)
 L R S E D T A V Y Y C A R L22582

CDR3-TPO
CCG ACC CTG CGC CAG TGG CTG GCG GCG CGC GCG CCG GTG TGG GGC CAG GGC ACC
 P T L R Q W L A A R A P V W G Q G T pAXB116 Fab'-gVh
 P T L R Q W L A A R A P V W G Q G T TT-Vh(CDR3-TPO)

ACC GTG ACC GTG AGC AGC
 T V T V S S pAXB116
 Fab'-gVh
 T V T V S A TT-Vh(CDR3-TPO)

Fig 24 Sequence of the pAXB116 Fab' Heavy chain variable region. The cDNA sequence with the best E. coli codon usage (Henaut and Danchin, 1996) and the translated amino acid sequence of pAXB116 Fab' are shown. CDR (Complementarity Determining Region) are defined by Kabat et al(1992) and the structural variability definition sequence (Chothia and Lesk, 1987) underlined and overlined, respectively. TPO peptides in heavy chain CDR2 and CDR3 of pAXB116 Fab' are indicated by double underlines and wavelines respectively. pelB leader cDNA sequences are overlined. pAXB116 Fab'-gVh denotes heavy chain variable region of human germline derived pAXB116 Fab'.

Figure 25

pAXB116 Fab' gV_k

(SEQ ID NO. 160) pelB leader ATG AAA TAC CTA TTG CCT ACG GCA GCC GCT GGA TTG TTA TTA CTC GCT GCC CAA
 (SEQ ID NO. 161) M K Y L L P T A A A A G L L L L A A A Q

pelB leader
 CCA GCC ATG GCG GAA ATT GTG CTG ACC CAG AGC CCG GGC ACC CTG AGC CTG AGC
 P A M A E I V L T Q S P G T L S L S pAXB116 Fab'-gV_k
 (SEQ ID NO. 162) E L T Q S P G T L S L S TTV_k
 (SEQ ID NO. 170) B I V L T Q S P G T L S L S X12686

CDR1-L1
 CCG GGC GAA CGC GCG ACC CTG AGC TGC CGC GCG AGC CAG AGC GTG AGC AGC AGC
 P G E R A T L S C R A S Q S V S S S pAXB116 Fab'-gV_k
 P G E R A T L S C R A S H S V S R A TTV_k
 P G E R A T L S C R A S Q S V S S S X12686

TAT CTG GCG TGG TAT CAG CAG AAA CCG GGC CAG GCG CCG CGC CTG CTG ATT TAT
 Y L A W Y Q Q K P G Q A P R L L I Y pAXB116 Fab'-gV_k
 Y L A W Y Q Q K P G Q A P R L L I Y TTV_k
 Y L A W Y Q Q K P G Q A P R L L I Y X12686

CDR2-L2
 GGC GCG AGC CGC GCG ACC GGC ATT CCG GAT CGC TTT AGC GGC AGC GGC AGC
 G A S S R A T G I P D R F S G S G S pAXB116 Fab'-gV_k
 G T S S R A T G I P D R F S G S G S TTV_k
 G A S S R A T G I P D R F S G S G S X12686

GGC ACC GAT TTT ACC CTG ACC ATT AGC CGC CTG GAA CCG GAA GAT TTT GCG GTG
 G T D F T L T I S R L E P E D F A V pAXB116 Fab'-gV_k
 G T D F T L T I S R L E P E D F A V TTV_k
 G T D F T L T I S R L E P E D F A V X12686

CDR3-L3
 TAT TAT TGC CAG CAG TAT GGC AGC AGC CCG TGG ACC TTT GGC CAG GGC ACC AAA
 Y Y C Q Q Y G S S P W T F G Q G T K pAXB116 Fab'-gV_k
 Y Y C Q Q Y G G S P W F G Q G T K TTV_k
 Y Y C Q Q Y G S S P X12686

GTG GAA ATT AAA
 V E I K
 Fab'-gV_k
 V E L K

pAXB116

TTV_k

Fig 25 Sequence of the pAXB116 Fab' Light chain variable region. The cDNA sequence with the best E. coli codon usage (Henaut and Danchin, 1996) and the translated amino acid sequence of pAXB116 Fab' are shown. CDR (Complementarity Determining Region) are defined by Kabat et al(1992) and the structural variability definition sequence (Chothia and Lesk, 1987) underlined and overlined, respectively. pelB leader cDNA sequences are overlined. pAXB116 Fab'-gV_k denotes light chain variable region of human germline derived pAXB116 Fab'.

Figure 26 - Primers to generate pAXB116 heavy chain

UDEC1709 : 5' primer 272 bp, containing NcoI site (5GQQ ID No. 163)

5'-CCAGGCCA⁷GGCGCAGGTGCA¹¹GCTGGTGCAGAGCGGGCGGAAGTGA¹⁵AAACCGGGCAGCAGCGTGA¹⁹AGT
GAGCTGCA²³AAAGCGAGCGGCGG²⁷CACCTT³¹AGCAGCTATGCGATTAGCTGGGTGCGCCAGGCGCCGGG³⁵CAGGGCTG
GAATGGATGGGCGG³⁹CATTATTCG⁴³ATTTGGCACCGCGA⁴⁷ACTATGCGCAGAA⁵¹ATT⁵⁵CAGGGCCG⁵⁹GTGACCATTAC
CGCGGATGAAAGCACCAGCACC⁶³CGTATATGGAA⁶⁷CTGAGCAGCC⁷¹TGCG ---'

Overlapping with UDEC1710

UDBC1710 3' primer 271 bp

5'—GTTCAGCTCACGGTACCGGAAATACTTTCACCAGGAGCCAGCGCCGCGGTGCGCGG
Overlapping with UDEC1711

CTGGTGTCTTGTCTGGGCCAGCGAAACACGCTGGGCTTGGTCTGGCTGCTACGGTACGGTGGT
GCCCTGGGCCACACCGGCCGGCGCGCCAGGGCACTGGCGCAGGGTGGCTTCAATCGGCAGGCCGCGCAA
TAATACACCGGGTATCTTCGCTGGCAGGGCTGCTCAGGTCATA—3' (SEQ ID NO. 164)
Overlapping with JIDEC1700

Overlapping with UDEC1709

OBESTRIN 5' primer (274 bp) containing XbaI site

5'—CGAGTCAGATTACGGGCGGCCAGCAGTTCCGGCGCGGGCACGGCGGGCAGGTATGGTTTATCGCAGCT
 TTCCGTTCCACTTTTATCCACTTTGGTGTGTCGGTTATGGTTCAGTTGCAAATATAGGTCTGGGTGCCAGG
 CTGCTGCTGGCAGGTCAACCAGCTGTCAGGTATACAGGCGCTGCTGCAAGCACCGGCCGAAAGGTATGCAC
 GCGCTGGTCAGCGCGCCGCTGTCAGCTCACGGTCACGGTTC—3' (Seq ID No. 165)
 overlapping with UDEC1710

overlapping with UDEC1710

Figure 27 - Primers to generate pAXB116 –light chain

UDEC1712 5' primer 236 bp

5'-CCAGGCCATGGCGGAAATTTGTGCTGACCCAGAGCCCCGGGCACCCGTGAGCCTGAGCCGGGCGAACGGCGAC
CCTGAGCTGCCGCGAGCCAGAGCGTGAGCAGCAGCTATCTGGCGTGGTATCAGCAGAAACGGGCCAGGGCGCG
CGCCCTGCTGATTTATGGCGCGAGCAGCCGGCGACGGGATTCCGGATCGCTTACGGGAGCGGCAGGGCAGGGCACCG
ATTTTACCCGTGAC-3' (SEQ ID NO. 166) Overlapping with udec1713 (24bp)

Overlapping with udec1713 (24bp)

UDEC1713 3' primer 239bp

5'-CTTCGCTTCGGCGGGATAAAAGTTGTTCAAGCAGGCACACCCAGCTCGGGTGCCGCTTTTCAGTGTTCA

overlapping with UDEC1714

TEGCTCTGGGGAAAAATAAAACAGGCTGGGGGGCCACGGTGGCTTAATTCCACTTGGTGGCTGGCAAAGGT
 CCACGGGTGCTGCCATACTGCTGGCAATAACACCGCAAAATCTCCGGTTCAGGGGCTAATGGTCAGGGTAA
 AATCGGTGCGCTG-3' (Seq ID No. 167) Overlapping with udec1712(24bp)

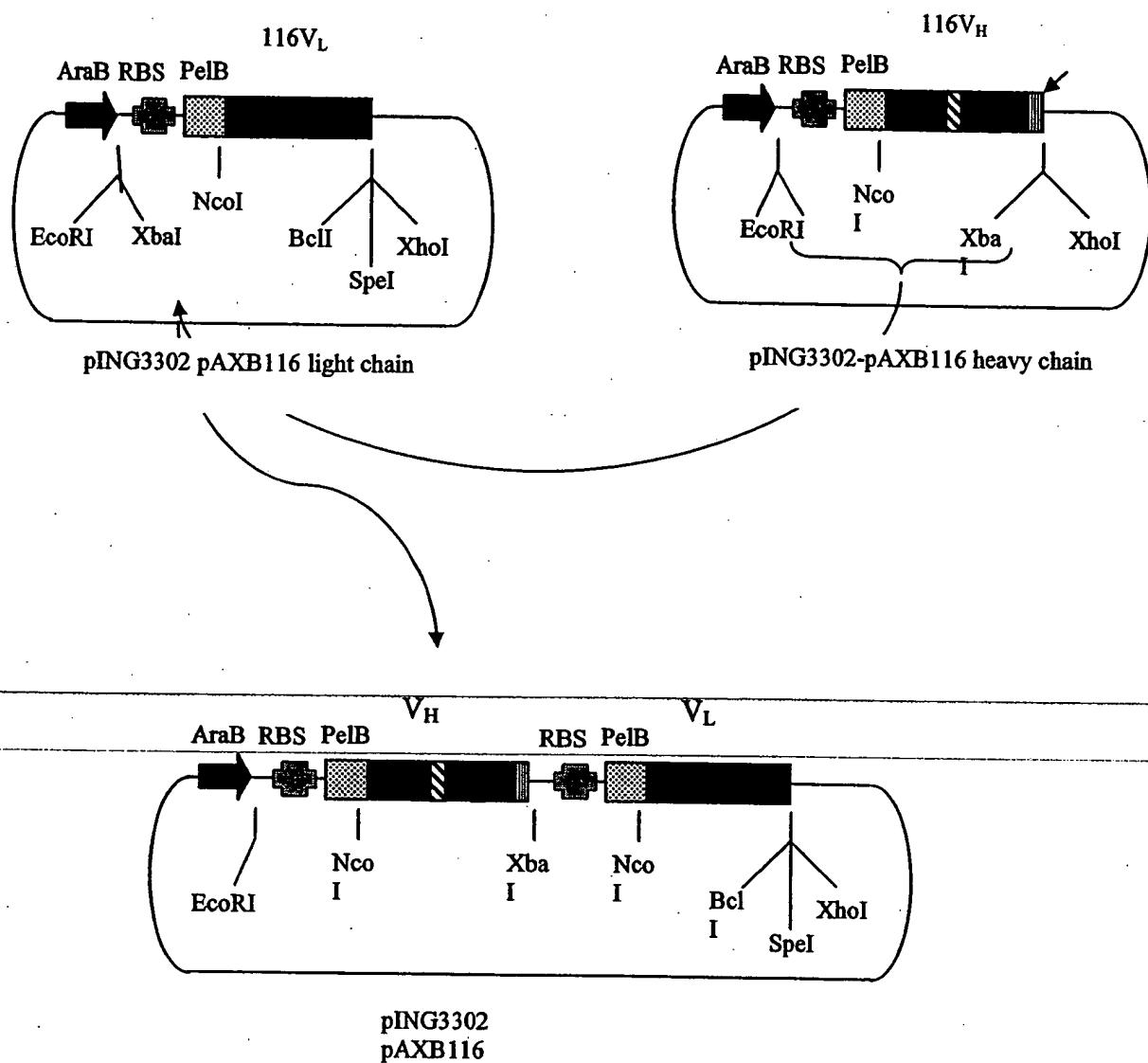
Overlapping with `udec1712(24hr)`

UDEC1714 3' primer 245 bp

5'—GTGCTGATCATTTAGCATTCGCCGGTTAAAGCTTTGGTCAACGGCAGGCTCAGGCCCTGATGGGTCACTTC
GCACGCATACACTTATGTTTCTATAATCGCTTGGTCAGGGTCTGGCTCAGGGCTATAGGTGCTATCTT
GCTATCCTGTTGGTCACGCTTCTGGCTGGCTGCGCTCTGAGCGCTTATCCACTTCCACTGCACTTCGCTTCG
CGCGGATAAAAGTIG—3' (SEQ. ID no. 168) overlapping with udec1713 (26 bp)

Figure 28

Construction scheme for pING-pAXB116



116 Light Chain (SEQ. ID NO. 122):

EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSG
SGSGTDFLTISRLEPEDFAVYYCQQYQGSSPWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGT
ASVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLKADYEKHKVYA
CEVTHQQLSLPVTKSFNRGEC.

Variable Region of 116 Light Chain (SEQ. ID NO. 123):

EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIPDRFSG
SGSGTDFLTISRLEPEDFAVYYCQQYQGSSPWTFGQGTKVEIK

116 Heavy Chain (SEQ. ID NO. 124):

QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAIWVRQAPGQGLEWMGQLIEGPTLRQWLA
ARANSRVTITADESTSTAYMELSSLRSEDTAVYYCARLPIEGPTLRQWLAARAPVWGQGTTVTV
SSASTKGPSVFPLAPSSKSTGGTAALGCLVKDYFPEPVTVWSNSGALTSGVHTFPAVLQSSGL
YSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKK { **VEPKSCDKTHTCPPCP** } *APELLGGP*

end CH1 constant domain hinge region tail region

Variable Region of 116 Heavy Chain (SEQ. ID NO. 125):

QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAIWVRQAPGQGLEWMGQLIEGPTLRQWLA
ARANSRVTITADESTSTAYMELSSLRSEDTAVYYCARLPIEGPTLRQWLAARAPVWGQGTTVTV
SS

Clone 116. The light chain sequence is as given. The heavy chain may have several forms depending on the final antibody form. For example: the minimum sequence ending with the CH1 constant domain may result in Fab assembly but the heavy chain/light chain interaction will not be stable. Commonly, a portion of the hinge region containing a cysteine (the underlined bold portion of hinge region) may be included for a covalent interaction between the heavy and light chains. Fab'2 association would need further cysteines such as an entire IgG1 hinge region (bold). In this example, clone 116 was cloned in a Xoma pING3302 modified vector which includes a transition tail region (italicized).

Fig. 29

Figure 30

SDS-PAGE of pAXB116, culture supernatant was resolved from each other by non-reducing 4-12% SDS-PAGE (lane "Sup") and cell lysate by reducing 4-12% SDS-PAGE (lane "Lysate"). Proteins were transferred onto Hybond Nitrocellulose Sheet (Amersham) and block with TBS-0.2% Tween-20+10% (w/v) Carnation nonfat dry milk. PAXb116 were detected by HRP-conjugated goat-antiHuman (H+L)Ab (Chenicon Cat#AP112P, (Temecula, CA). The signals were detected by ECL.

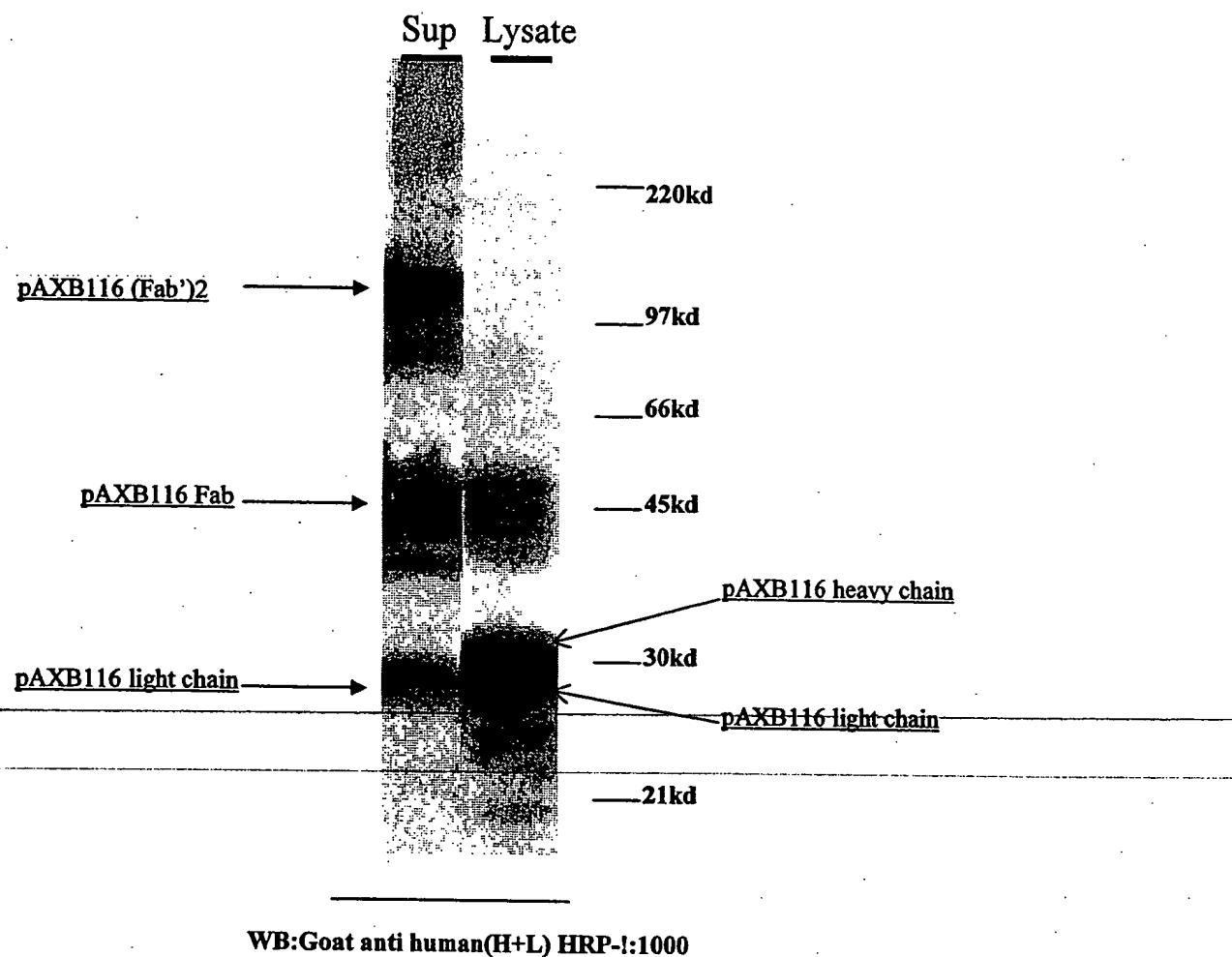


Fig. 31

Proliferative Effect of TPO on CD 34+ Cord Blood Cells

CD34⁺ cord blood cells (Poeisis) were thawed, washed, resuspended in BIT9500 serum-substituted medium (StemCell Technologies, Inc.), and plated at 3.5×10^5 per well in a 96 well flat-bottom plate with increasing concentrations of either recombinant human TPO (R&D Systems), circle, or pAXB116, square. After four days of culture at 37°C in a 5% CO₂ incubator, 1 μ Ci of ³H thymidine (Perkin Elmer) was added to each well and cells were further incubated for 16 hours. Cells were harvested with an automatic 96-well cell harvester. ³H incorporation was measured using a betaplate liquid scintillation counter (Wallac). Proliferation of cord blood cells are measured as counts per minute (CPM) and CPM values are an average of three wells.

Proliferative Effect of TPO and 116 on CD 34+ Cord Blood Cells

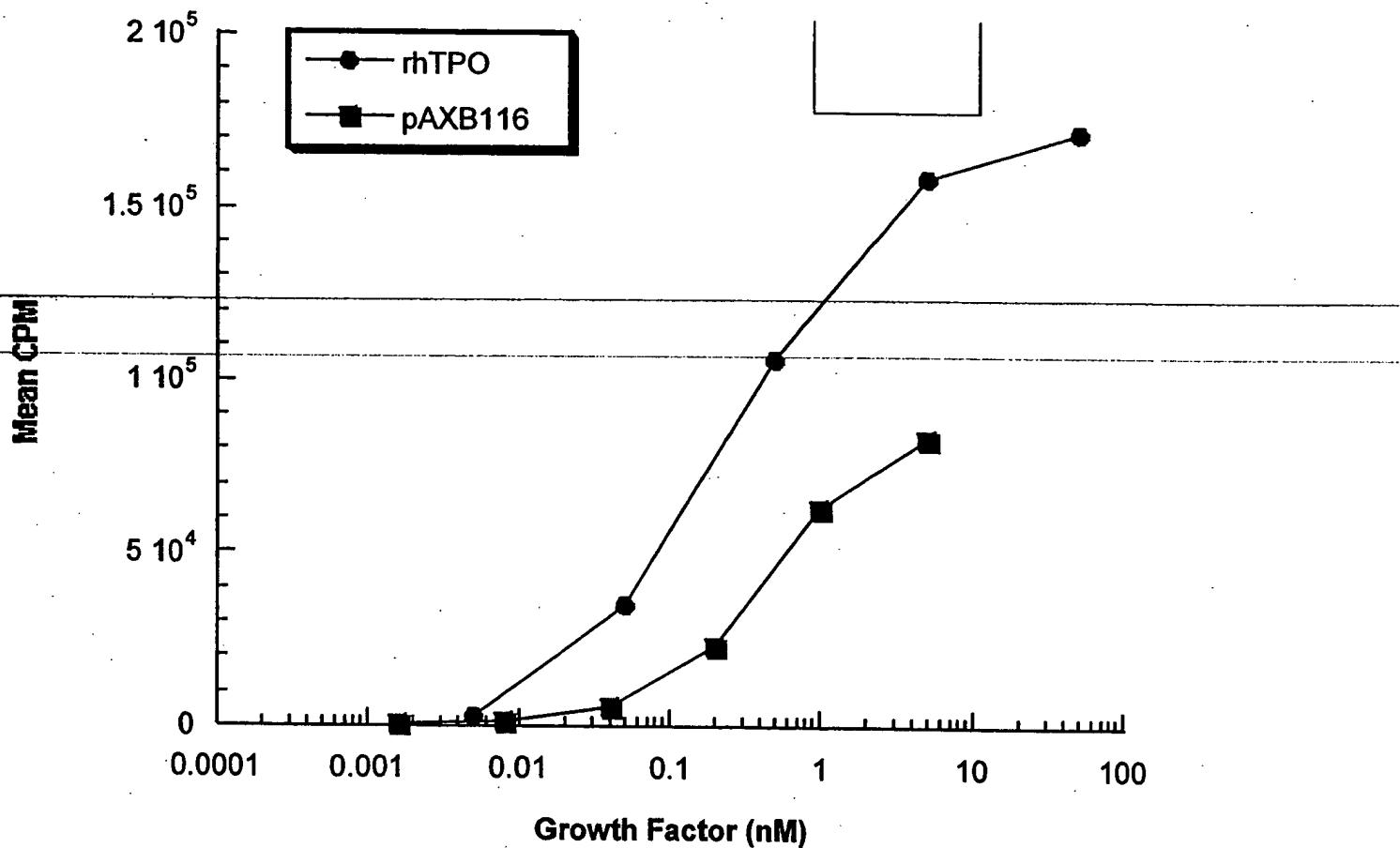


Figure 32: Activity of 116 Fab' prep #5

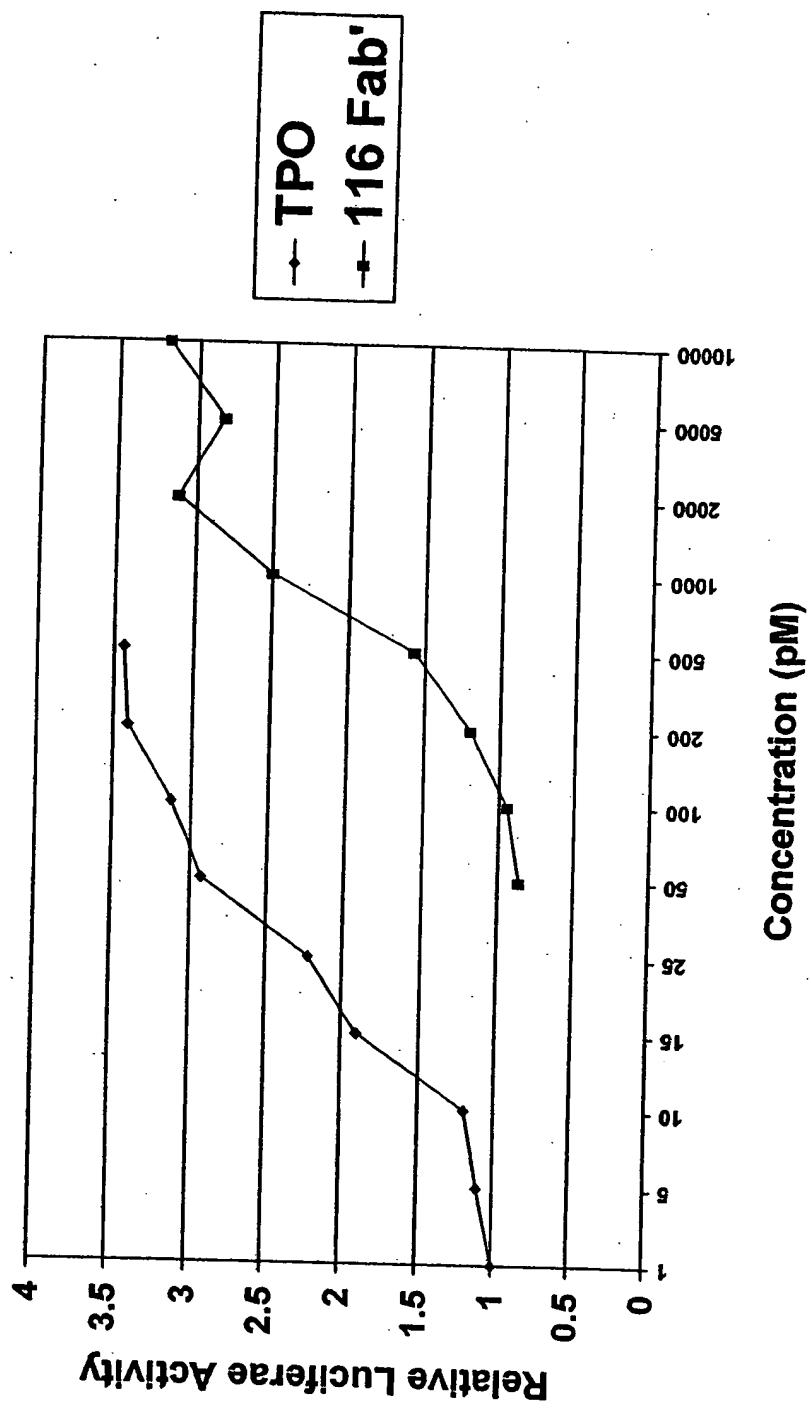


Figure 35

Sample Sequences of Heavy Chain CDR2 clones

Gly-Ile-Phe-xxx-xxx-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-xxx-xxx-Gly (SEQ. ID NO. 126)
TT backbone randomized TPO peptide randomized TT backbone

<u>Clone</u>	<u>Amino Acid Sequence</u>
HR2-14	Gly-Ile-Phe-Ser-Pro-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Gly-Gly (SEQ. ID NO. 127)
HR2-20	Gly-Ile-Phe-Pro-Gln-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Lys-His-Gly (SEQ. ID NO. 128)
HR2-23	Gly-Ile-Phe-Pro-Asn-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Thr-Gly-Gly (SEQ. ID NO. 129)
HR2-28	Gly-Ile-Phe-Lys-Gly-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Pro-Gly-Gly (SEQ. ID NO. 130)
HR2-43	Gly-Ile-Phe-Pro-Pro-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Ala-Val-Gly (SEQ. ID NO. 131)
HR2-44	Gly-Ile-Phe-Pro-Arg-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Lys-Leu-Gly (SEQ. ID NO. 132)
HR2-48	Gly-Ile-Phe-Pro-Arg-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Lys-Leu-Gly (SEQ. ID NO. 133)
HR2-50	Gly-Ile-Phe-Pro-Tyr-Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leu-Ala-Ala-Arg-Ala-Lys-Arg-Gly (SEQ. ID NO. 134)

Figure 34 Relative Activity of 2° H2/H3-(X4b) clones

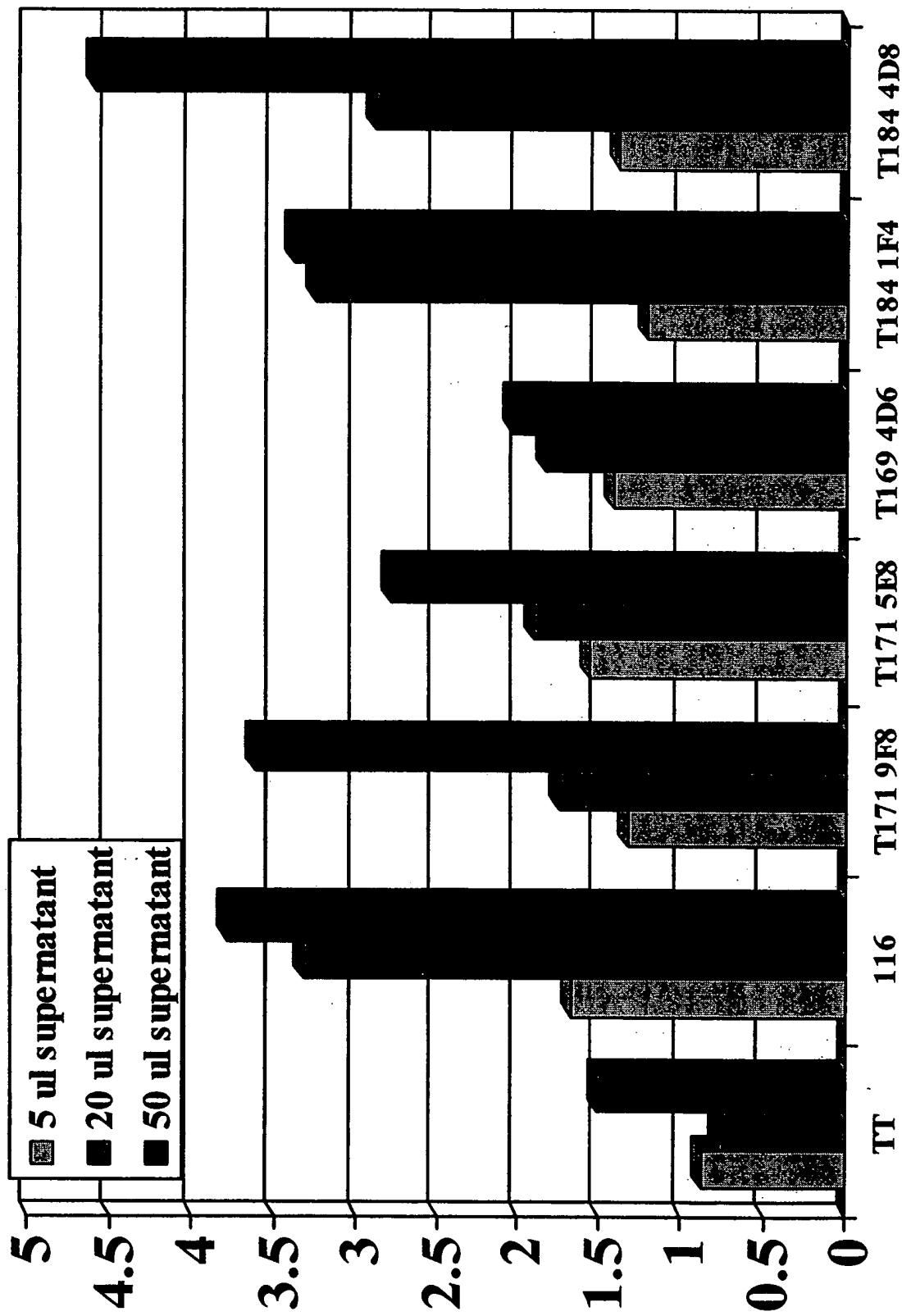


Figure 35: Optimization of the TPO placement in HC-CDR2

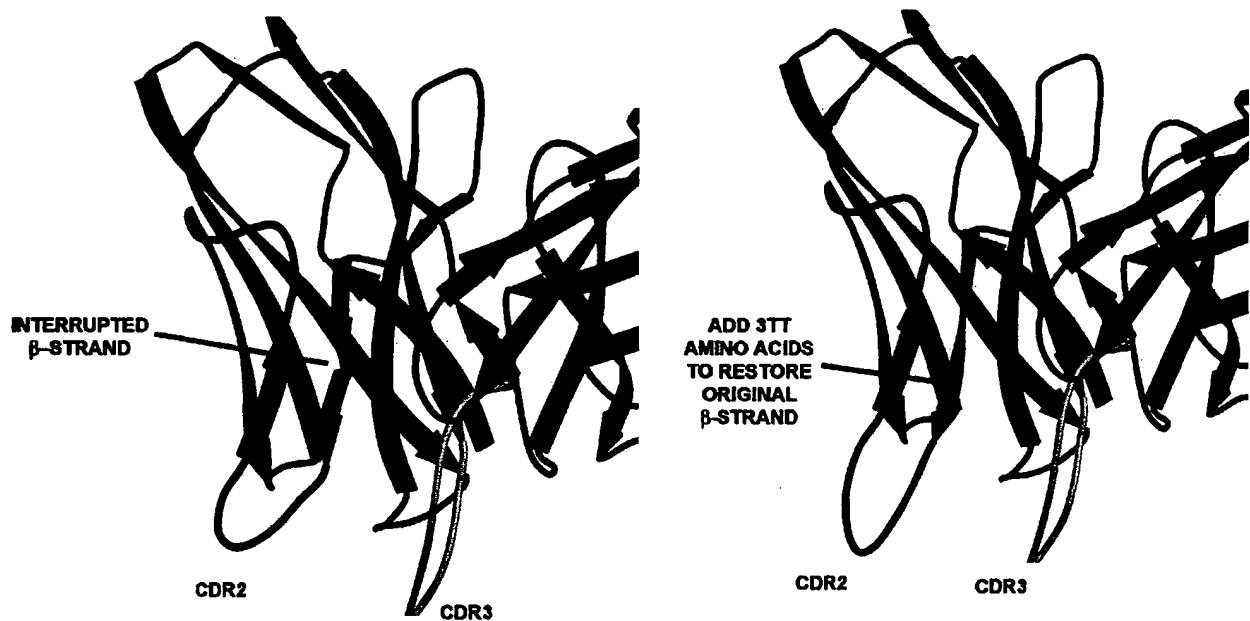


Figure 36A (seq. ID. no. 141)

Figure 36B

GACAACGATCGGAGGACCEAAGGGAGCTAACCGCTTTTGCAACACATGGGGATCATGTAACCGCTTATCGCTTATCGTGGAAACCGAGCTGAATGAAGCC
 CTGTTGCTAGCTCCGGCTCTCGATGGCAAAAACGTGTTGACCCCTAGTACATTGAGCGGAACCTAGCAACCTTGGCTCGACCTTACTTGG
 BsrGI BsrDI AdII FspI
 ATACCAAAACGAGCTGTACACCACGATGCCGTAGCAATGGCAACACGTTGCGAAACTATTAACCTGCGAACTACTTACTCTAGCTTCCGGCAAC
 TATGGTTGCTGCTGACATGTGGCTACGGACATCGTACCGTTGTTGCAACCGCTTATAATTGACCGCTTGTGAATGAGATCGAAGGGCGTT
 12C
 AseI Ecl BglII
 ATTAATAGACTGGATGGAGGCAGATAAAGTTGAGGACCACTTCTGCGCTCGGCCCCCTCGGCTGGCT66TTTATTGCTGATAAACTGGAGCCGGTGA
 TTAATTATCTGACCTACCTCGCCATTCAACGCTCTGGTGAAGACGGAGCCGGACCAAAACGACTATTAGACCTCGCCACT
 13C
 BpmI BsaI BsrDI BmrI AhdI
 GCGTGGGTCGGCGGTATCATTGAGCACTGGGCCAGATGGTAAGCCCTCCGTATCGTAGTTATCTACACGACGGGAGTCAGGCAACTATGGATGAA
 CGCACCCAGAGGCCATAGTAACGTCGTGACCCGGTCTACCATCGGGAGGCATAGCATCAATAGATGCTGCCCTCAGTCGTTGATACCTACTT
 14C
 DraI
 CGAATAGACAGATGCTGAGATAGGTGCCACTGATTAAGCATTGGTAACTGTCAGACCAAGTTACTCATATATACTTTAGATTGATTAAACCTC
 GCTTTATCTGCTAGCGACTCTACCGGAGTACTAATTGTAACCATTGACAGTCTGGTCAAAATGAGTATAATGAAATCTAACTAAATTGAG
 15C
 DraI BspHII
 ATTTTAATTAAAGGATCTAGGTGAAGATCCTTTTGATAATCTGATGACCAAAATCCCTAACGTGAGTTTGTCCACTGAGGGTCAGAGCCCGT
 TAAAGATTAATTCTCAGATCCACTCTAGGAAAAACTATTAGAGTACTGGTTTGGAAATTGCACTCAAAAGCAAGGTGACTCGCAGTCGGGCA
 16C
 AGAAAAGATCAAAGGATCTCTTGAGATCTTTCTGCGCGTAATCTGCTGTTGCAACAAAAACCCGCTACCGGGTGGTTGTTGCC
 TCTTTCTAGTTCTAGAAACACTAGGAAAAAGAGCGCATTAGACGAGGAACTGGTTTGGTGGCATGGTCGCCACCAAAACAGGCG
 17C
 Eco57I
 GATCAAGAGCTACCAACTCTTCTCGAAGGTAACCTGGCTCAGCAGAGCGAGATACCAAATCTGCTCTAGTGTAGCCGTAGTTAGGCCACCACT
 CTAGTCTCGATGGTGAGAAAAAGGCTTCATTGACCGAAGTCGTGCGCTATGGTTATGACAGGAAGATCACATGGCATATCCGGTGGTGA
 18C
 AMNI
 TCAAGAACTCTGTAGCACCCCTACATACCTCGCTCTGCTAATCCTGTTACCAAGTGGCTGCGCAAGTGGGATAAGTCGTTCTTACCGGGTTGGACTC
 AGTTCTTGAGACATCGTGGCGATGTATGGAGCGAGACGATTAGGACAATGGTACCGACGCGTACCGCTATTCAAGCACAGAATGGCCCAACCTGAG
 19C
 ApaI
 AAGACGATACTTACCGATAAGGCAGCGGTGGCTGAAACGGGGGTTCTGCAACACGCCAGCTTGAGCGAACGACCTACACCGAACTGAGATAAC
 TTCTGCTATCAATGGCTTCTCGCGTCGCGCAGCCGACTTGGCCCTTCAAGCACGTTGCGGGTCGAACCTCGCTTCTGAGTGTGCTTACTCTATG
 20C

Figure 36c

Figure 50D

Figure 36E

Bpu10I BstEII

TATATAGCCTGAGCAGCGTGGTACCGTGGCGAGCAGCCTGGGACCCAGACCTATTTGCAACGTGAAACCATAACCGAGCAACACCAAAGTGGAA
ATATATCGGAACTCGTGGCACCACTGGCACGGCTGGTCTGGATATAACGTTGCACTTGGTATTTGGCTCGTTGGTTAACCT 41C

L Y S L S S V V T V P S S L G T Q T Y I C N V N H K P S N T K V D
codon optimized CH1

NgoMIV
BglII
SmaI
SphI
MscI
NaeI
FseI

TAAAAAAAGTGGAAACCGAAAAGCTGGATAAAACTAGTGGCCAGGGCGGCCAGCACCATCACCATGGCGCATACCGCTACGACGTTCGGACTAC
ATTTTTTCACTTGCTTTTCGACGCTATTTGATEACGGTCCGGCGCTGCTGGTAGTGGTAGTGGTACCGCGTATGGCATGCTGCAAGGCCTGATG 42C

K K Y E P K S C D K T S G Q A G Q H H H H H H H G A Y P Y D V P D Y
codon optimized CH1 Linker His 6 tag HA tag

GCTCTTAGGAAGGGTGGTGGCTCTGGGGTGGCGGTTCTGAGGGTGGCGCTCTGAGGGAGGGCGGTTGGGTGGCTCTGGTCCGGTATTTGATT
CGAAGAACCTCCACCAACCCGAGACTCCCACCGCCAAAGACTCCACCGCCGAGACTCCCTCCGCAAGGCACCCACCGAGACCAAGGCCACTAAACCTAA 43C

(seq ID no. 171)

A S E G G G S E G G G S E G G G S G G G S G S G D F D
gene III fragment

ATGAAAAGATGGCAACGCTAATAAGGGGCTATGACGGAAAATGCCATGAAAACGCGCTACAGTCTGACGCTAAAGGAAACTTGAATTCTGTCGCTAC
TACTTTTCAACGTTGGATTATTCCCGATACTGGCTTACGGCTACTTTGGGATGTCAGATGGGATTTCGAACAGACAGCATE 44C

Y E K H A N A N K G A M T E N A D E N A L O S D A K G K L D S V A T
gene III fragment

Clai

TGATTACGGTGCTGCTATCGATGGTTTGATTGGTACGTTCCGGCCCTCTAAATGGTAATGGTCACTGGTAGTTGGCTCTAAATTCCAAATG
ACTAATGCCACGACGATAGCTACCAAAAGTAACCACTGCAAAGGCCGAAACGATTACCAATTACACGATGACCACTAAACGACCGAGATTAGGGTTAC 45C

D Y G A A I D G F I G D Y S G L A N G N G A T G D F A G S N S Q H
gene III fragment

XbaI BsaXI SspI BsaXI

GCTCAAGTCGGTGACGGTGTATAATTACCTTTAATGAATAATTCCGGTCAATATTACCTTCCCTCCCTAAATGGTTGAATGTCGCCCCTTTGTCTTA
CGAGTTCACTGCCACTATTAAAGTGGAAATTACTTAAAGGCAAGTTAAATGAAGGGAGGGAGTTAGCCAACCTACAGGGAAACAGAAAT 46C

A Q V G D S D N S P L M N N F R Q Y L P S L P Q S V E C R P F V F
gene III fragment

NheI NheI

GCGCTGGTAAACCATATGAATTTCGATTTGATTTGAGCAAAATAAACCTATTCCGGTGGTGTGTTGGCTTGTGTTATATGTTGCCACCTTATGTTATG
CGCGACCATTTGGTATACTTAAAGATAACTAACACTGTTTATTTGAATAAGGCACCAAGAGAAACGCAAGAAAATACAAACGGTGGAAATACATA 47C

S A G K P Y E F S I D C D K I N L F R G V F A F L L Y V A T F M Y V
gene III fragment

AflII NheI AseI Nofl BglII

ATTTCTACGGTTCTAACATACTGCGTAATAAGGAGTCTTAAGCTAGCTAAATTAAAGCGGCCGCAAGATCTGCTCTGAGGAGGATCT 4783

TAAAAGATGCAAACGATTTGATGACGCATTCTCAGAATTGATCGATGATTAATTAAATTGCGCCGGCTAGACGAGAGACTCCTCTAGA

F S T F A N I L R N K E S
gene III fragment

Figure 37 Relative Activity of 116 Mutants

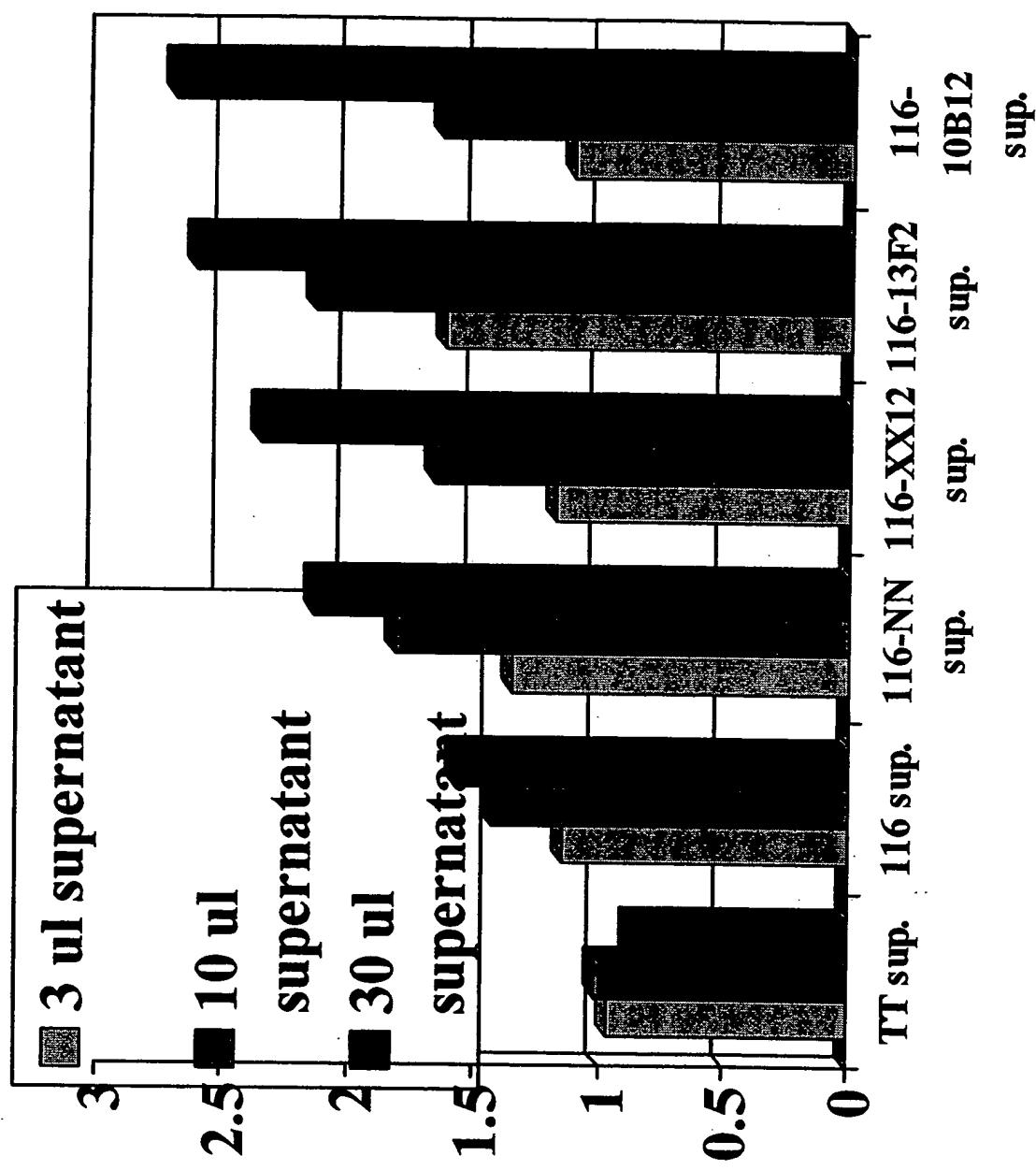


Figure 38 116 Variants Alignment

	10	20	30	
1	Q V Q L V Q S G A E V K K P G S S V K V S C K A S G G T F S			pRL5-116 (VH)
1	Q V Q L V Q S G A E V K K P G S S V K V S C K A S G G T F N			pRL5-116 NN (VH)
1	Q V Q L V Q S G A E V K K P G S S V K V S C K A S G G T F G			pRL5-116 10B12 (VH)
1	Q V Q L V Q S G A E V K K P G S S V K V S C K A S G G T F Q			pRL5-116 13F2 (VH)
1	Q V Q L V Q S G A E V K K P G S S V K V S C K A S G G T F P			pRL5-116 XX12 (VH)

	40	50	60	
31	S Y A I S W V R Q A P G Q G L E W M G Q L I E G P T L R Q W			pRL5-116 (VH)
31	N Y A I S W V R Q A P G Q G L E W M G Q L I E G P T L R Q W			pRL5-116 NN (VH)
31	E Y A I S W V R Q A P G Q G L E W M G Q L I E G P T L R Q W			pRL5-116 10B12 (VH)
31	D Y A I S W V R Q A P G Q G L E W M G Q L I E G P T L R Q W			pRL5-116 13F2 (VH)
31	R Y A I S W V R Q A P G Q G L E W M G Q L I E G P T L R Q W			pRL5-116 XX12 (VH)

	70	80	90	
61	L A A R A N S R V T I T A D E S T S T A Y M E L S S L R S E			pRL5-116 (VH)
61	L A A R A N S R V T I T A D E S T S T A Y M E L S S L R S E			pRL5-116 NN (VH)
61	L A A R A N S R V T I T A D E S T S T A Y M E L S S L R S E			pRL5-116 10B12 (VH)
61	L A A R A N S R V T I T A D E S T S T A Y M E L S S L R S E			pRL5-116 13F2 (VH)
61	L A A R A N S R V T I T A D E S T S T A Y M E L S S L R S E			pRL5-116 XX12 (VH)

	100	110	120	
91	D T A V Y Y C A R L P I E G P T L R Q W L A A R A P V W G Q			pRL5-116 (VH)
91	D T A V Y Y C A R L P I E G P T L R Q W L A A R A P V W G Q			pRL5-116 NN (VH)
91	D T A V Y Y C A R L P I E G P T L R Q W L A A R A P V W G Q			pRL5-116 10B12 (VH)
91	D T A V Y Y C A R L P I E G P T L R Q W L A A R A P V W G Q			pRL5-116 13F2 (VH)
91	D T A V Y Y C A R L P I E G P T L R Q W L A A R A P V W G Q			pRL5-116 XX12 (VH)

	121	121	121	121	121	
121	G T T V T V S S (SEQ. ID No. 147)					pRL5-116 (VH)
121	G T T V T V S S (SEQ. ID No. 148)					pRL5-116 NN (VH)
121	G T T V T V S S (SEQ. ID No. 149)					pRL5-116 10B12 (VH)
121	G T T V T V S S (SEQ. ID No. 150)					pRL5-116 13F2 (VH)
121	G T T V T V S S (SEQ. ID No. 151)					pRL5-116 XX12 (VH)